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THE PREMARITAL EXAMINATION

Paul Scholten, M.D., San Francisco

The premarital examination required by law is sometimes cursory, sometimes thorough; in any case it brings the bride and groom to the physician. Although the gynecologist is uniquely fitted for premarital counseling, the general practitioner is at present the one most frequently consulted. The interview cannot follow a set pattern because of the diversity of situations encountered, and in some cases more than one interview is necessary. The premarital examination here outlined consists of laboratory studies, general evaluation of medical history and sexual knowledge, general physical examination, a pelvic examination, and a conseling session. Circumstances do not always permit immediate answers to all questions, but many informative books are now available. From the list here given, the physician should choose some that most nearly represent his own convictions, so that he can recommend them in such cases. To a physician who is sufficiently interested and has adequate time and training, the premarital examination is an opportunity to help substantially to preserve the American family life.

DUE TO THE almost universal adoption of compulsory premarital health examination laws by the various states, the premarital blood test has become an accepted part of preparation for marriage in America today. Starting with Connecticut in 1935, to date 46 of the states have passed such laws. These statutes are primarily measures for the control of infectious venereal disease and, in most instances, require a serologic test only. However, some of the states require an additional physical examination, aimed at detecting primary syphilitic lesions, even though the disease has not yet progressed to a point evidenced by a positive blood test.

These premarital examination laws bring the bride and groom to the doctor. Once there, the premarital examination they receive can be purely cursory and consist simply of the blood test or it can consist of a complete medical examination in the full sense of the term. It is such an examination that is herein outlined, for, while the premarital examination is usually initiated only to fulfill legal requirements, it also offers the physician an opportunity to be of genuine service to the patient and to the community.

An increasing number of marriages are ending in divorce. Statistics show that one of four marriages will not survive for five years. In some localities this figure may rise as high as one out of three. In addition to those couples who actually get to the divorce courts, there must be a reasonable per-

From the Department of Obstetrics and Gynecology, University of California School of Medicine.
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centage of unhappy marriages that are never resolved in an attorney's office. While not all divorces or unhappy marriages arise from a sexual basis, a surprisingly high percentage do have their origin in some disagreement at that level. Although we can only surmise as to how many cases of incompatibility and mental cruelty fall within our field, we as physicians can help to cut down the number of unsuccessful marriages by giving more attention to counseling before marriage in the hope of eliminating some of the frustrations and points of conflict before they arise.

Not all couples who are happy in the most intimate act of marriage are compatible in other interests, but it is certainly safe to state that those who are unhappy in their sexual relations are usually unhappy with most other aspects of their marriage as well. On a medical level, we can only estimate how much marital strife shows up in a doctor's office as pelvic pain syndromes, menorrhagia, dyspareunia, fear of pregnancy, and other similar psychosomatic disorders. Certainly, many of these complaints could be prevented or minimized by adequate premarital counseling. Such counseling is a specialized field for which the physician, and in particular the gynecologist, is logically fitted by his background and training.

At present a number of organized groups offer short courses and conferences in family relations for the newlyweds or the about-to-be-married; these include various church denominations, the Y. M. C. A., educational institutions, and planned parenthood foundations. In addition, many of our colleges and universities now give family relation or marriage courses to the undergraduate students. All of these agencies, while doing good work, tend to be impersonal, generalized in subject matter, and unavailable to the vast majority of the population at the particular time when they are most needed—the immediate prenuptial period.

On the other hand, the physician should be the logical man to carry out such counseling since he is readily available, should be fully understanding, and is specifically trained for the job. By virtue of his specialty, the gynecologist is uniquely fitted for premarital counseling and increasing numbers of prospective brides are now coming first to gynecologists for examination. At present, however, most premarital examinations are done by the general practitioner, and this may be appropriate inasmuch as he examines both prospective bride and groom and can correlate their individual problems. He is frequently already one or the other's family doctor and has established the good rapport needed for intimate advice. But it is important that a proper gynecologic approach to the problem be used too and that adequate premarital counseling be done at the time of premarital examination. Occasionally the psychiatrist should become a part of the counseling team but usually only when he is called in consultation because of some major, deep-seated emotional problem related to the marriage.

Premarital counseling should be preventive medicine, aimed at warding off causes of future disagreement by means of advice, instruction, and education. As Pearson [1] has pointed out, it differs from marriage counseling, which aims at patching up a marriage already in danger of break-up and which requires specialized legal and psychiatric knowledge. Premarital counseling needs only basic gynecologic training, plus interest and adequate time on the part of the doctor.

When the prospective bride does come to the doctor, how is he to manage the consultation? It has been suggested that the best counseling relationship be an informal one and that no set pattern be followed but rather that the patient be allowed to ask questions and to direct the counseling toward the subjects she desires. Unfortunately, this would be time consuming and, with a nervous or frightened patient, the essential subjects may never be covered. Preferable is the use of a basic outline for an adequate premarital examination so that essentials can be covered in logical sequence.

Easley [2] suggests that the premarital examination should involve three office visits. A brief preliminary visit is made which is confined to generalizations and nonmedical subjects in order to put the patients at ease and to set the stage. At this time the blood test is taken or ordered but no actual examination is done. On the second visit the physical and pelvic examinations are done, but it is not until the third visit that conclusions and advice are given and the prospective husbands seen. If the consulting physician does not treat males, he may refer them for general history, physical examination, and serology and then later counsel with them as indicated.

This plan presupposes that the premarital advice will be sought at an ideal time four to six weeks before the wedding, but, unfortunately, most couples wait until the last moment or at least the last week before initiating the medical examination. Although most gynecologists are pressed for time, certainly with a basic plan in mind they can do a praiseworthy job in a single consultation of about 25 to 30 minutes. To help to accomplish this, I would like to suggest an outline of an adequate premarital examination consisting of (1) laboratory studies, including the required serologic test for syphilis, (2) general medical history and sexual-knowledge evaluation, (3) a thorough physical examination, (4) a pelvic examination, and (5) advice and counsel.

Outline for Examination

Laboratory Studies.—The serologic test for syphilis is mandatory and usually is the only laboratory work demanded; however, additional laboratory

tests that are often used to complete a premarital medical survey include Rh factor determination, hemogram, urinalysis, and a chest film.

History.—A brief general medical history should be taken. Most of the premarital patients seen will be in a young, generally healthy age group, but the usual review of past illnesses, accidents, operations, systemic and familial illnesses, and anomalies is important. Menstrual history should be carefully elicited and patterns established. The last menstrual period may be important in regard to the actual date set for the wedding. Menstrual physiology may be reviewed as an aid to judging the woman's knowledge of her bodily functions. This logically leads to an evaluation of her sexual knowledge and experience. This evaluation can be casual and brief, consisting of a few simple questions, or it can be quite formal and detailed.

About 50 to 60% of women seen in premarital consultation will be virgins and a number more will be near-virgins with limited sexual experience. One should ascertain past sexual activities and, even with the virgin, discreetly question about prior attempted sexual contacts and possible traumatic experiences. Of note at this point are the 10 to 25% of brides who will already be pregnant at the time of marriage. Your whole scheme of advice will have to be changed by this. It is wise for preserving your own composure and that of the patient if you refrain from detailed advice about first intercourse and the wedding night until you find out if she is pregnant.

Most women in this day and age will have some knowledge of sex, even if they have had no actual experience. Some will have been previously married, widowed, or divorced, and a history of this should be obtained. Almost all will have read one of the many available books on sex and marriage by the time you are consulted. Many, however, will not have absorbed very much from their reading; some will have absorbed only misconceptions; and some will remain completely ignorant of what the marital act actually involves. Preliminary questioning at this point serves to bring this out and to establish a basis for advice to be given later.

For a more detailed, formal evaluation, several excellent interviewing aids devised by Dr. Gelolo McHugh of the department of psychology of Duke University are available from the Family Life Publications, Inc., of Durham, N. C. These are the "Sex Knowledge Inventories," form X and form Y, questionnaires that the patient fills out before the interview. Form X is an objective measure of sex knowledge through 80 multiple-choice questions covering the whole field involved in marriage counseling. Form Y measures individual understanding of sex vocabulary and anatomy through labeled diagrams and matching-type questions. These forms can be used independently or together. They are a counseling tool which may be helpful in saving time and in giving a basis for discussion by pointing out the areas of knowledge where counseling is most needed. Their successful use depends more on the counselor than on the tests.

Whether by formal questionnaire or informal discourse, some sort of sexual history should be taken if the physician is able to elicit it. He should also question about parental marital life and parental attitudes toward marriage, children, and sex. The child is the mirror of the parents and thus many families perpetuate mistakes and unhealthy attitudes from generation to generation.

Physical Examination.—After the maximum knowledge is gained from the history, a complete general physical examination should be done to rule out general or systemic disease.

Pelvic Examination.—The pelvic examination is essential, with especial attention paid to hymenal presence, dilation or dilatability, discharges, cervicitis, polyps, Trichomonas or Candida (Monilia) infections, pelvic anomalies, developmental defects, possible senile changes, childbirth injuries, or any other variations from the normal.

Kavinoky[3] suggests that, at this point, when examining a girl of no or little experience, the insertion of a plain laboratory size Pyrex test tube, well lubricated, will help the patient to realize that there is a normal opening in the hymen and that it leads to a normal deep vaginal canal. This will demonstrate better than words can the normal vaginal axis and capacity. If a contraceptive device is to be fitted, it should be done at this time.

Occasionally at the time of pelvic examination, we will find a thick, rigid, or imperforate hymen. We can help this condition by office dilation or, rarely, surgical hymenotomy or hymenectomy, but the latter should be reserved for only the most serious cases. Much worse for the bride than a tight hymen is a tender area of healing for three to six weeks after surgery.

If the patient has several weeks remaining until the wedding, it is best to accomplish dilation in the office with the gradual use of a well-lubricated set of graduated dilators. If she has only a minor degree of tight or thick hymen, advice may be given on how to use adequate water soluble lubricants or one of the less sensitizing anesthetic lotions to help her ease the initial discomfort of intercourse. This anesthetic lotion, at the same time, may be valuable in controlling premature ejaculation in the male. Usually, nature is the best dilator and should be given a fair trial. In some cases, Kegel exercises, used over a period of several weeks to months, may be of aid in securing relaxation.

After the physical examination, the patient is told to dress and is then seen in the consultation room for the actual counseling and advice. Any

findings or details of technique for intercourse should not be discussed while the patient is still on the table.

Advice and Counseling

By choice, the counseling should be fairly extensive. If for any reason it must be minimal, allow at least a short time for answering specific questions that have arisen, and then, certainly, direct the patient to adequate available literature for sources of more complete answers.

For the busy physician there are a number of source materials available in the form of pamphlets or books which may be dispensed or recommended to the patient. Several of the pharmaceutical companies put out booklets giving a small amount of advice on marital hygiene and sex, but these booklets are mostly inadequate and often are only thinly disguised advertisements. A more adequate and more to be recommended pamphlet is a reprint of a very popular editorial from the journal, *Obstetrics and Gynecology* (4:355-360 [Sept.] 1954) titled, "A Young Woman Seeks Premarriage Counsel" by Dr. C. O. McCormick. This is a well written article in first person style which has gone into many printings and which may be purchased at a nominal price from Paul B. Hoeber, Inc.

There are a number of other pocket-sized manuals on sex and marital guides, each 75 to 100 pages in length, which are available to the physician for 60 to 75 cents a copy if purchased in bulk. These have been written with the intention that the doctor should dispense them at the time of the premarital examination. These manuals contain information on basic anatomy, physiology, sexual technique, and contraception. They serve to round out the physician's advice but each booklet contains some controversial information, and the individual physician would do well to read them carefully before recommending them in order to make sure that the contained information coincides with his own ideas. These pocket-sized books include "Sex Without Fear" by S. A. Lewin and John Gilmore, "A Doctor's Marital Guide" by Bernard Greenblat, and "Sex Manual" by G. Lombard Kelly.

Other more formal volumes which may be recommended for further study include "A Marriage Manual," Hannah and Abraham Stone, "Modern Pattern for Marriage," Walter Stokes, "When You Marry," Evelyn Duvall and Reuben Hill, "Successful Marriage," Morris Fishbein and Ernest W. Burgess, "Facts of Life and Love," Evelyn Duvall, "Sex Factors in Marriage," Helena Wright, "Before You Marry," Sylvanus Duvall, "Marriage Is What You Make It," Paul Popenoe, "Marriage for Moderns," Henry Bowman, "Marriage and Sexual Harmony," Olive Butterfield, "Building a Successful Marriage," J. T. Landis and M. G. Landis, "A Handbook for Husbands and Wives," Theodore Arden, "Family Living," Evelyn Duvall, "Personal Adjustment, Marriage and Family Living," J. T. Landis and M. G. Landis, "Marriage and Family Relationship," Robert Foster, and "Marriage," Robert Harper.

What are the usual questions a young woman wants answered when she comes for premarital advice? These usually include such topics as (1) whether she is generally healthy and physically able to bear children; (2) facts regarding family planning, regulation of fertility and conception; (3) detailed sexual information regarding techniques and hygiene and a chance to ask specific questions about these; and (4) legal requirements.

The physical and pelvic examinations certainly should enable the physician to reassure the patient about her physical well-being and probable fertility. Family planning or regulation of fertility is one of the larger elements in the premarital counseling and often is the reason for selecting a gynecologist. Very few couples, given the choice, desire a pregnancy immediately after marriage. Generally speaking, it is better if there can be a short period before pregnancy ensues, in which time the couple can make the necessary adjustments to sex relationships, finances, and other aspects of marriage. It is often hard for two young people to adjust to each other under ordinary circumstances, but it is much more difficult when one of them is suffering from morning nausea, malaise, and the increased irritability that may come with pregnancy.

However, it is advisable for the doctor to caution against waiting too long to have children, especially the older age groups. Too often couples postpone pregnancy year after year for reasons of finances, education, and housing, only to find they have an infertility problem when they do attempt conception. In general, contraception, by whatever method, should not be prolonged for more than two years at most. Advise, too, that failure of conception, when attempted, calls for prompt medical consultation and corrective study as soon as possible, preferably within 6 to 12 months.

Detailed methods of contraception are too well known to devote space to them here. The physician must always keep in mind the couple's religious and ethical beliefs, and it is not for him to lay down any standard of conduct. He must merely advise and counsel. The amount of counseling the physician may give couples depends to a considerable extent on their own needs and questions. Scheffey [4] has noted that some couples are healthy and emotionally mature individuals, looking forward to the joys and companionship of marriage. Others have physical problems; while still others are normal physically but unstable and underdeveloped emotionally. The amount of counseling also depends on the physician's own maturity and interest and how well he can convey an interesting and intimate body of advice.

Specific Points of Advice

Libido.—It should be pointed out that while both sexes are equally capable of enjoying the sex act, the libido differs from men to women. Men are usually ready for sex with minimal stimulation, while women are usually less interested in sex as such, taking a more natural or matter-of-fact attitude. Hollywood, television, modern magazines, and novels have all led men to glamorize sex. Women can enjoy sex as much as men do, but they are usually not aroused as quickly nor as easily. Many times women wonder what men get so excited about. While a man may become aroused at the sight of a tight sweater, the same is certainly not true of most women. As a general rule, the average woman is less interested in sex and will be satisfied with sex about half as often as her spouse is. This is especially true if she has small children and the labors of a busy household. Of course, this is less likely in the early months of marriage when the young couple is free to devote all of their time to pleasing each other.

Frequency of Intercourse.—Questions concerning frequency of intercourse are commonly asked. We as physicians must once again be careful about laying down any specific rules or limitations. We can advise that there is no set pattern for the first six months or so because that is a time of trial, experiment, and mutual adjustment. We can say that after this approximate length of time, most couples settle down to a pattern of intercourse about twice a week, occasionally three to four times a week, but that this is only an average estimate and the number is an individual matter of mutual demand, agreement, and satisfaction.

Orgasm.—The orgasm or climax is a mysterious subject to most prospective brides. While about half will have had some prior sexual experience, the majority will not have experienced orgasm. Most, however, will have read of the orgasm and found it described as vital to sexual and marital happiness. Most authors have difficulty in explaining what orgasm actually is; and it is indeed hard to describe such a vivid but almost entirely emotional experience. If the girl is a follower of Hollywood, true confession magazines, or Hemingway, she may well expect orgasm to be accompanied by a flash of lightning, a roll of thunder, and a small earthquake. If so, she will most certainly be disappointed and may not even recognize the event when it does happen.

The difference in a man's orgasm and a woman's orgasm can best be explained by saying that in the male there is an actual emission which gives a definite end or climax to the act; in a woman, however, orgasm is merely a lessening of tension after a building up of warmth, emotion, expectancy. This comes as a sudden release with an accompanying feeling of pleasure, warmth, love, togetherness, and relaxation. Orgasm in both can be likened to a sneeze in which there is a building up of tension and of expectancy and then of release. The physiological points of increased pulse, increased blood pressure, more rapid respiration, and then the slowing down of all these may be pointed out. But perhaps in the end we must agree with a local doctor who counsels, "If you have to ask what an orgasm is, you haven't had one; if you do experience orgasm, you won't have to ask." We can also explain that after intercourse and orgasm, the couple is usually relaxed, happy, and ready for sleep.

Further explain that the normal man will experience orgasm each time he has intercourse, but in general a woman will achieve it only about half as often. This latter fact is due to several factors: 1. The woman is generally more slowly aroused and if the husband is hasty, clumsy, inattentive, or inexperienced, he may be finished before the wife is more than mildly interested in what is happening. 2. Orgasm requires both relaxation and concentration on the part of the woman. If she is tired, nervous, or afraid of pregnancy, still upset from a busy day or family life, she may not be able to relax. If privacy is lacking, as it is with couples living with in-laws, or who have children in the same room or nearby, or have neighbors or television or radio in the next room or flat, concentration is practically impossible and a successful climax is usually denied. It may take many months after the honeymoon for a woman to acquire enough relaxation and concentration to achieve orgasm. If this is not explained to the bride-to-be in advance, initial experiences may lead her to frustration rather than to enjoyment.

It is ideal if both parties reach orgasm at the same time, but this is only the ideal and is neither essential nor usual. As stated, the wife usually experiences a climax only about half as often as her spouse does. Occasionally a woman will be more easily aroused, but, on the other end of the scale, perhaps 10% of women will never experience an orgasm throughout their married lives. We can warn the prospective bride of this but should hasten to add that, even without orgasm, a marriage relationship can be a beautiful and successful one. The sex act can still be a pleasure, a sharing of intimacy, a pleasurable warmth, and a joy in making a loved one happy. While there may be no abrupt climax, there can be an enjoyable building up of tension and a gradual release from it. Closeness can give satisfaction even without orgasm and we should give reassurance about this.

Actual techniques of intercourse may be touched on without undue emphasis. Point out that there are only four basic positions. While some of the more sensational guide books point out innumerable atti-

tudes, in reality all are only minor variations of these basic four. None of these are either more normal or more abnormal than others; nor should variations in sex technique be a cause of embarrassment to either of the newlyweds. The first few months of the marriage are ones of experimentation and trial in all fields of mutual living and sex is no exception. It is important to point out here that there is no absolute line of normality or abnormality in regard to the sex act. Anything that gives mutual satisfaction to both parties is normal. That which one party finds unnatural or unpleasant or disgusting or abnormal, is abnormal.

Frigidity.—Frigidity is a special problem but usually is not part of the premarital consultation save as a fear on the part of the bride. This fear usually implies prior unhappy experience. Most frigidity is on a purely emotional level and is very rarely physical. All we can do is to sincerely reassure the patient that there is no physical bar to successful intercourse and to emphasize the fact that within a few months time marital adjustment will usually provide the relaxation and relief of tension needed to solve the problem. Some mild cases of fancied frigidity will be aided by small doses of testosterone over a six-week period. This therapy seems to help emotionally and it will certainly cause some clitoral hypertrophy. True frigidity, however, is primarily a problem calling for psychiatric assistance. Of course if there is a physical bar to successful coitus, such as a rigid hymen or a tender introitus, we can and should offer therapy.

It is most important that the wife be able to discuss sex frankly with her husband if they are to achieve mutual satisfaction and success in marriage. She should never simulate orgasm just to please her husband since honesty is vitally important in this most intimate aspect of marriage.

We can suggest that occasionally the wife should initiate the sex act. This is flattering to the man and strengthens his opinion of his own value and desirability. Conversely, she should refuse only rarely to have intercourse, since in this she is rejecting that which her spouse considers the most valuable and personal thing he has to offer her. She should not be ashamed of sex. Intercourse is not intended solely for pregnancy but for pleasure as well. For a successful marriage, a woman must be many things to her spouse—a good cook, a housekeeper, a mother to her husband, and a good mistress as well.

General Points of Information

We should try to correct certain implied psychological threats by pointing out that it is not true that the hymen must break painfully and bleed to prove virginity; that it is not true that compatibility is proved by simultaneous orgasm; that this is ideal, but unlikely; that the husband is not directly responsible for the wife's orgasm, although the friction does cause the stimulus initiating orgasm; that orgasm is more a mental and an emotional reaction than a physical one on the bride's part.

There are certain personal matters that should be touched on. Most newlyweds will be living in small apartments and of necessity be thrown into very constant intimate contact. In such a close atmosphere, it is important that they keep their bodily functions personal; for example, they should keep the bathroom door closed when so occupied and in turn respect each other's privacy. Sanitary napkins and belts and douche bags are best kept under cover. The bride should be advised against lounging around in an old dressing gown or in her underwear. Occasionally the half-dressed form is an exciting thing to see, but in general nudity removes the mystery and cheapens and coarsens the interpersonal relationships. Daintiness in a woman is still a virtue and an intensely attractive aspect.

Douching might be mentioned at this point. Most girls about to be married will not have had occasion previously to use a douche. Explain that a routine douche is not necessary, but an occasional postcoital or postmenstrual douche may be desirable. For this purpose a simple vinegar and water douche should be sufficient, and it would be wise to explain how to douche in the bathtub or on the toilet.

We should give the patient an opportunity to ask specific questions which our counseling has raised or has left out. We can point out that the physician is usually a better source of premarital advice than are well-meaning friends.

Now arises the problem of the pregnant bride. This is a common one, since approximately 10% of all women are pregnant when wed. Kinsey [5] and others raise this percentage to as high as 20 and 25%. Under these circumstances, reassurance is the most important therapy we have to offer. Telling the girl that her plight is not an uncommon one is a valuable adjunct. It can be more comforting to her if you point out how rare it is that anyone ever makes an untoward remark to the mother of an 8-lb. "premature." Naturally, anyone who can count will be able to figure out what has happened but, in general, friends and relatives will prove to be surprisingly compassionate in this regard. It is sometimes wise to reassure the girl that she has done the right thing to decide to be wed, once she has made her own decision. It is equally important that the doctor not make the decision for the patient. Instead, he can point out the various courses open, and there will be numerous cases where placing the infant for adoption may be far preferable to a shotgun wedding.

The divorcee or the widow who is about to be remarried will usually know the basic facts about sex and obviate the need for a formal lecture or list

of details. However, it is just as important that she be given a chance to ask any questions she desires answered, since prior marriage is no proof of adequate ability to adjust to marriage.

Marriage in later life poses several problems. While pregnancy is less likely to occur, if it does, it is also more prone to bring complications. After the menopause there is an actual shrinkage of tissues, loss of elasticity, and loss of lubricating secretions. Advise gentleness of techniques in intercourse in order to avoid tearing of tissue and advise the use of lubricants, of which the water soluble ones are best. For some patients, local or generalized estrogenic substances are advisable and, in some cases, the anesthetic lotions or ointments may be helpful.

One final word may be said about preparing for the actual wedding and the honeymoon. Modern marriage is more conservative than some would have us think; it still retains much of the ritual and mysticism of our primitive ancestors. What with showers, fittings, rehearsals, bachelor parties, the ceremony and the reception, a wedding can become an almost barbaric rite. By the end of the usual ordeal, the bride and groom may both be in a state of near-collapse, both mentally and physically. The treatment must be individualized to the patient, but quite often a course of one of the simpler tranquilizers during the last prenuptial week will serve to help retain the bride's sanity. Meals usually become highly irregular, so a mild laxative nightly can also be helpful during these last few days before the wedding. A conscious effort on the part of the bride to force fluids will do much to help her cut down on honeymoon cystitis. Point out that it is not necessary to consummate marriage on the wedding night; often it is much better to wait until both parties are sober, rested, and relaxed.

Menstrual physiology can be touched on briefly or outlined as indicated by the evaluation made earlier or answers received when making the initial sex-knowledge inventory. Many young women are dismally unaware of their bodily functions and certainly those patients who refer to menstruation as the "curse" could stand a little missionary work. An outline of menstrual physiology forms part of the family-planning counseling and should be the basis for use of the so-called rhythm system or of the safe period.

If you are able to attain good rapport and assume a properly fatherly attitude toward the patient, there are a number of subjects that can be added as a part of the individual's technique of counseling, depending on how well the physician fits the role. Some of these subjects, while not an essential part of the counseling, can form an effective part of it if properly conveyed to the patient. Little things can be mentioned that tend to keep the romance of marriage alive and flourishing, such as remembering anniversaries, the parting morning kiss, avoiding quarrels, avoiding criticism of the spouse, making a 50-50 partnership of the marriage. Financial security and budgeting may be touched on. Religion should be discussed as a fundamental aspect of the family and the marriage and how the church should enter into the life of the new family. The imparting of these subjects is dependent on the counselor's gray hair and ability since they are interesting but not essential.

What is essential is the proper gynecologic approach and adequate counseling at the time of the premarital examination. The physician can help to preserve the American family life by premarital and marital counseling, by advice on child spacing and family planning, by good obstetric and gynecologic care. The ideal physician for this task should have personal warmth and sympathetic understanding, but basically he need have only interest, adequate time, and adequate training.

1975 Ocean Ave. (27)

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SOLAR CARCINOGENESIS.—Collagen degeneration of the skin arises in persons with inadequate cutaneous pigment from excessive exposure to solar radiation. By altering the nutrition of the epidermis, collagen degeneration predisposes to the development of solar keratoses, keratoacanthoma, squamous-cell carcinoma, and basal-cell carcinoma; when present in only moderate degrees it can intensify and accelerate other carcinogenic influences. Our final conclusion is that the carcinogenic effect of ultraviolet light is mediated by its primary action on the dermis. —B. S. Mackie, M.B., B.S., D.D.M., and V. J. McGovern, M.D., The Mechanism of Solar Carcinogenesis, *A. M. A. Archives of Dermatology*, August, 1958.

SUBTOTAL CYSTECTOMY AND TOTAL BLADDER REGENERATION IN TREATMENT OF BLADDER CANCER

Roger Baker, M. D., Timothy Kelly, M. D., Timothy Tehan, M. D., Charles Putnam, M. D.
and
Edouard Beaugard, M. D., Washington, D. C.

Three types of operation are particularly important in the treatment of cancer of the urinary bladder: transurethral resection, suprapubic segmental resection (which may be subtotal), and cystectomy. Considering the difficulty of complete extirpation of the lesion by transurethral route and the disadvantages of cystectomy to the patient, the authors are convinced that the former is too likely to prove inadequate and the latter unnecessary and too radical. In their experience nearly all of the bladder can be removed by the technique of suprapubic segmental resection without depriving the patient of the possibility of ultimately regaining good vesical function. The operative mortality is not greater in proportion to the amount of bladder wall removed, for the remaining portion has the ability to regenerate all the layers of the normal bladder. Such regeneration occurred in all patients, and bladder capacities up to 410 cc. were attained. The subtotal operation is preferred even in patients with cancer so far advanced that the operation must be regarded simply as palliative, for it removes a mass that is a source of pain and hemorrhage.

In 1953 one of us first reported the favorable results associated with subtotal cystectomy and bladder regeneration in treatment of 16 patients with bladder cancer.[1] This paper presents data collected from five years of additional experience with the procedure in treatment of bladder cancer of all stages and grades. Subtotal cystectomy should be evaluated from two aspects: first, rationale for use of this type of surgery, and, second, clinical data concerning bladder regeneration. These will be handled separately.

Rationale for Use of Subtotal Cystectomy

The three surgical methods used practically to the exclusion of all others in treatment of bladder cancer are transurethral resection, suprapubic segmental resection, and cystectomy. Essentially subtotal cystectomy is a large or radical segmental resection. In order to justify the use of a radical segmental resection, the present cure rate associated with standard segmental resection for superficial infiltrative or deep infiltrative bladder lesions should be equal to or better than that obtained by transurethral resection or total cystectomy.

Transurethral Resection.—Critical appraisal of transurethral resection as a therapeutic modality for superficial or deep infiltrated vesical cancers indicates that it falls short of the usually acceptable surgical techniques employed in treatment of malignancy. First, the operator is restricted in the extent of his resection by the possibility of perforating the bladder wall. For even small or superficial infiltrative bladder cancers the operator must not resect more than about 0.3 cm. beneath the tumor or he will cut a hole in the inflated bladder and have extravasation of the irrigating fluid into the retroperitoneal or intraperitoneal space.

This obligatory restriction of even local excision of a malignant tumor should be condemned. The fact that the cure rate of superficial infiltrating vesical cancers treated by the transurethral method is good should not deter the urologist from improving on these statistics. When a particular cancer in a particular patient is viewed through the resectoscope, the urologist is unable to determine whether that particular tumor will fall into the statistical group that can be treated successfully by transurethral resection. Due to this inability of prediction of depth of infiltration and circumferential spread of the cells within the bladder wall, each patient should be given the benefit of at least having the entire thickness of the bladder wall beneath the neoplasm excised with the tumor en bloc. This cannot be done by transurethral resection.

In previous reports, we have clearly demonstrated that certain bladder cancers of even a superficial nature can spread a considerable distance away from the lesion within the bladder wall and that this spread is not visible through the resectoscope.[2] Moreover, this spread of cancer cells within the bladder wall cannot be palpated at the time of exploration of the bladder via the suprapubic route. It was demonstrated that in certain cases considerably more than a cuff of "normal" bladder around the tumor must be excised to remove all cancer within the wall of the bladder. More recently we have observed that, even with superficial infiltrative lesions, tumor cells can be found in the adventitia or fat immediately adjacent to the bladder. It is

From the Department of Surgery (Division of Urology), Georgetown University School of Medicine.

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impossible to remove these cells by the transurethral resection method. In addition, as it is not possible to predict at the time of suprapubic segmental resection which patient requires a larger or smaller segmental resection, each patient should be given the benefit of the larger resection with full realization that the smaller resection would have cured a large number of the superficial infiltrating carcinomas. This approach is logical and valid provided the operative mortality of the larger segmental resection is no greater than that associated with the smaller segmental resection or the transurethral resection. In our studies and those of others with comparable but smaller series, the operative mortality is no greater.

From a statistical standpoint a review of the more recent significant results associated with treatment of superficial infiltrating carcinomas of the bladder by electro-excision demonstrates a five-year survival rate of about 67%.[3] Persons with tumors of similar stage and grade treated by segmental resection have a similar (66.3%) five-year survival rate.[4]

At this point another misconception should be corrected concerning this method of therapy. It has been stated that the reason transurethral electroexcision fails to cure some patients with superficial infiltrating carcinomas is that the tumors are multifocal in origin. This is usually not true. In actual practice most urologists use segmental resection for two types of patients: those initially seen with large lesions and those where previous transurethral resection has failed to cure and some more "radical" procedure must be used. The fact that the cure rate with segmental resection is so high indicates that the "multifocal cause of failure" attributable to the transurethral electro-excision method is not valid in most patients. One thing can be stated. If transurethral electroexcision is used in treatment of even superficial infiltrating bladder cancers, about 30% of these patients will die of their disease.

There is much evidence to indicate that the statistics associated with segmental resection are actually considerably higher than the mean of 66.3% reported in the more significant papers published to date. As stated above, most urologists do not utilize segmental resection for the smaller lesions. The procedure is reserved for the larger lesions which can be expected to have a poorer survival rate than smaller lesions. Again, most urologists do not utlize segmental resection in the initial treatment of these lesions. Thus, it is seen that many of the patients in the 66.3% survival rate group have previously had transurethral resection which has failed to cure the patient. The carcinoma at time of segmental resection, therefore, is one which has existed within the patient for a longer period of time. Such patients can be predicted to have a lower survival rate than those initially treated by the method. Disregarding these considerations, it can still be stated that segmental resection is equally as effective as transurethral resection for even superficial infiltrating carcinomas of the bladder. Based on all of the considerations mentioned, it is reasonable that if all of these superficial infiltrating carcinomas were treated by a larger segmental resection the present survival rate with the procedure could be increased.

Deep infiltrating carcinomas of the bladder treated by electroexcision have a five-year survival rate in the range of 12%.[3] When this same type of infiltrating carcinoma is treated by segmental resection, the published mean five-year survival rate is approximately 15.1%.[4] This last figure may be slightly higher than that which can be obtained in treatment of unselected cases with standard type of segmental resection. In any case, the statistics published to date indicate that segmental resection is at least as good, if not better, treatment than transurethral electroexcision for deep infiltrating carcinomas of the bladder.

Cystectomy.—Only a few urologists routinely perform total cystectomy for bladder cancer. Most urologists do not support the stand which states that cystectomy is absolutely necessary to effect cure of this disease. Some contend that if cystectomy is curative then a less radical procedure would also have cured the patient. Many firmly believe that the operative mortality associated with cystectomy cancels out the increased five-year survival rate that might be obtained with the procedure. Many urologists contend that the renal complications associated with cystectomy and transplantation of the ureters to the skin or functioning rectosigmoid, defunctionalized rectosigmoid, or ileal loop do not justify use of the procedure. If the cancer cure rate were sufficiently high after cystectomy and ureteral transplantation, the justification for making a significant percentage of these individuals "renal invalids" would be present. Moreover, these patients usually have some type of external collection apparatus for either urine or feces which certainly tends to make these individuals a type of urologic cripple, it not renal cripple.

Anyone practicing urology at an active university hospital where many postcystectomy referral patients are seen can attest that there is in fact much justification for these concepts concerning cystectomy and the results of diversion of the ureters. As a consequence it is not totally unreasonable that most urologists treat these patients with transurethral or segmental bladder resection. Complete pessimism concerning cystectomy is not reasonable, however, for recently the procedure has been generally used as a "last ditch" procedure for advanced bladder cancer. In the majority of the published reports, cystectomy was resorted to only after more conservative types of treatment had failed. As such, these patients must also be classified as failures for the conservative management. This is seldom

specified in published reports. Since most urologists perform relatively few of these operations, the incidence of operative mortality and complications of all types, including the renal variant, are greater than those of the few urologists who have much experience with the procedure. Actually, use of the ileal pouch for diversion of the urinary stream has fewer renal complications than formerly experienced with other types of ureteral transplantation. For those who have not performed the procedure, however, it should be remembered that the ileal pouch technique is a major operation in itself. The delayed renal complications usually associated with other methods of diversion of the urinary stream are lessened but not eliminated with the ileal pouch technique.

The present indications for total cystectomy have not been definitively established. Of more importance is that the necessity for cystectomy, as compared to segmental resection to effect cure, has not been proved. There are apparently only two

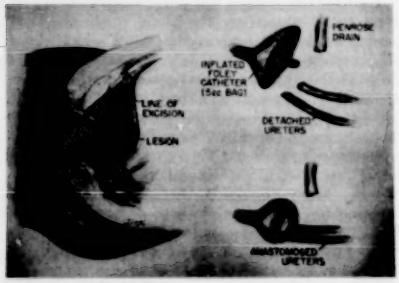

Fig. 1.—Subtotal cystectomy with reanastomosis of ureters; residual bladder sufficiently large to close over inflated 5-cc. Foley bag catheter; regeneration complete in three to eight weeks.

exceptions to this stand, namely, multifocal vesical cancer and infiltrative lesions immediately at the vesical neck. Both require cystectomy. Superficial infiltrating carcinomas of the bladder treated by cystectomy have a mean five-year survival rate of 43.3%.[3] Lesions of this same group treated by segmental resection have a mean five-year survival rate of 66.3%,[4] indicating that segmental resection may well be a better surgical method of treatment than cystectomy for these superficial infiltrating lesions. Deep infiltrating cancers treated by cystectomy have a mean five-year survival rate of 9.9%.[3] This same type of lesion treated by segmental resection has the higher five-year survival rate of 15.1%.[4] Cystectomy is usually selected for the larger lesions. Such tumors can be predicted to have a lower survival rate. These comparative percentage rates, therefore, are probably closer to each other than the statistics indicate.

Regardless, for the superficial or deep infiltrating bladder cancers, cystectomy offers the patient little more, perhaps less, than can be obtained with the standard simple segmental resection. In addition, patients having segmental resection are not subject to having their urine or feces drain into a collection apparatus attached to the abdominal wall. Current statistics, therefore, do not justify the opinion that "poor" or "inadequate" cancer surgery has been performed if anything less than cystectomy is used in treatment of superficial or deep infiltrative vesical cancer. The statistics do indicate that segmental resection is equally as curative, if not more so, as total cystectomy. This is applicable for all but the two exceptions previously mentioned of multifocal or bladder neck cancer.

Conclusions.—Apparently cystectomy is unnecessary and too radical a procedure. Transurethral resection is inadequate treatment to achieve maximum potential cure rate for bladder cancer for all stages and grades. This leaves segmental resection as the most desirable of the three methods. Based on these considerations and statistics, we have been exploring the possibilities of subtotal cystectomy for treatment of bladder cancer in an effort to improve the present favorable statistics obtainable with segmental resection.

Bladder Regeneration After Subtotal Cystectomy

We have demonstrated that after subtotal cystectomy in the dog, the entire bladder wall regenerated. We first reported clinical use of this remarkable regenerative ability of the urinary bladder in 1953.[1] In the human as well as the dog, the new bladder is composed of all layers seen in the normal bladder. From a clinical standpoint, regeneration always occurs except if the urine is diverted from the area. The regeneration into the form of a hollow viscus is due to an unknown chemical inductor in the connective tissue matrix immediately beneath the epithelium of the urethra at the vesical neck or the terminal ends of the adjacent ureters or both.

Procedure.—In order to study the procedure of subtotal cystectomy and bladder regeneration, cancers at various sites in the bladder and of varying stage and grade were included in the series on an unselected basis. All patients with papillomas were excluded from the series. Treatment was classified as palliative only when the cancer had spread beyond the bladder to the pelvis or to multiple lymph nodes or chest or bones.

A diagnosis of cancer was established in each patient by a transurethral resection of the entire lesion with the patient under general anesthesia. This general rule of complete transurethral resection of the lesion was adhered to throughout the study with the exception of huge bladder cancers. In this latter situation biopsies of multiple areas were performed with the resectoscope. After resection of the cancer, the entire base of the lesion,

including a 1-cm. margin peripheral to the edge of the lesion, was electrocoagulated. Four to seven days later subtotal cystectomy was performed. Based on location, size, and depth of infiltration of the cancer, varying percentages of the bladder were removed. The precise amount of excision had to be determined at time of operation, for endoscopic appearance and bimanual examination were of little assistance. Lesions of low grade and low stage usually resulted in excision of only about 30 to 50% of the bladder. Lesions of moderate grade and moderate stage which were larger in circumference were excised by the subtotal technique in which all but a piece of the bladder was removed. Regardless of amount of vesical excision, whenever possible a small piece of the bladder was salvaged as it accelerated regeneration and resulted in a larger definitive bladder (fig. 1). In all patients the peritoneum attached to the bladder, the perivesical fat, and the bladder segment were removed en bloc.

As the objective of the operation was to excise cancer, no attempt was made to salvage one or both ureteral orifices if doing so would appear to compromise adequate excision of the lesion. Consequently, one or both of the orifices were often sacrificed. The ureter or ureters were reanastomosed to the remaining bladder segment just prior to complete closure of the segment. A standard fish-mouth ureteroneocystostomy was performed.

In most patients it was possible to close the remaining bladder segment, regardless of its shape, over an inflated 5-cc. bag of a Foley catheter. In 12 patients, it was impossible to close the residual bladder segment due to its small size. In these patients the ends of the ureter or ureters were spatulated and anastomosed to the edge of the residual piece of bladder with a single suture (fig. 2). In a few patients with lesions at the vesical neck even this small bladder segment had to be excised, thus resulting in total cystectomy. The ureters of these latter patients were managed in one of two ways: A large isolated segment of rectosigmoid was anastomosed to the urethra, the proximal end of the segment was closed, and the ureters were sutured into this piece of colon. Continuity of intestine was established with standard end-to-end closure. In several male patients, however, true total regeneration of the bladder developed as the ends of the ureters were spatulated, and by a single suture each was attached to the anterior rectal wall as close as possible to the urethra (fig. 3).

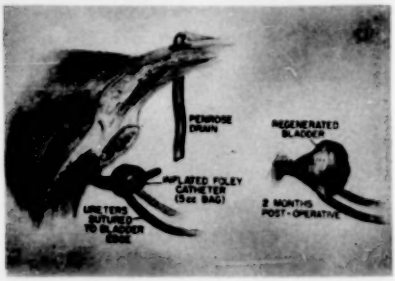

Fig. 2.—Subtotal cystectomy; remaining bladder not large enough to close; ends of ureters spatulated and sutured to open bladder segment; regeneration complete in 4 to 12 weeks.

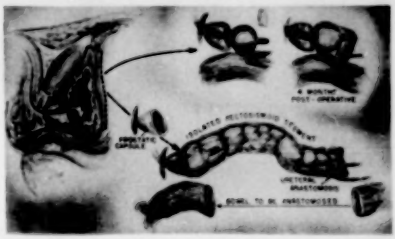

Fig. 3.—Total cystectomy demonstrating alternate methods of ureteral management used. Note peritoneum and perivesical fat excised with bladder.

In all patients an empty Penrose drain was inserted through the abdominal wound to the bladder or the bladder area. As the pelvic peritoneum had been excised with the lesion, the pelvic floor could not be reperitonealized in any of the patients. The Penrose drain was removed approximately four to seven days after suprapubic urinary drainage had stopped and one day after removal of the urethral catheter. If suprapubic drainage persisted for longer than 14 days, the drain was removed. The catheter was left in place for four to seven days after suprapubic drainage ceased.

Results

Essentially this method of management of bladder cancers consists of two surgical procedures: a preliminary complete transurethral resection of the lesion followed by a subtotal cystectomy. It has been of interest to study these subtotal cystectomy specimens. Such specimens of some superficially infiltrating lesions, as determined by the earlier transurethral resection, have later demonstrated that tumor cells were present in the adventitial lymphatics or lymphatics of the bladder wall some distance from the site of the original lesion. It was particularly disquieting to observe cancer cells in adventitial lymphatics when meticulous search of the transurethrally resected cancer site failed to reveal any residual cancer (fig. 4). While only a few such cases were observed in this study they represent definite, conclusive failure of cure by transurethral resection of superficial infiltrating

cancer. These patients tend to support our earlier observations relative to the circumferential spread of cancer within the lymphatics of the bladder wall.[2] These findings also prompted institution of our existing program in which peritoneum and perivesical fat as well as the bladder segment with

Fig. 4.—Carcinoma in lymphatic of perivesical tissue (× 300).

its tumor are removed in a block as this fat or adventitia surrounding the bladder may contain cancer cells.

No intestinal complications resulted from inability to reperitonealize the pelvis. Peritonitis did not complicate the postoperative course. Ileus has been a troublesome factor in several patients but has never been greater than that observed in certain individuals after routine renal surgery. Early in the study two ward patients probably developed unsuspected electrolyte imbalance which became fatal. Electrolyte imbalance is assumed as no demonstrable cause of death was detected at autopsy. No subsequent ward or private patients have died from electrolyte imbalance. No electrolyte imbalance has been seen that required significant treatment. One private patient with a deeply infiltrative epidermoid (squamous cell) carcinoma died of a pulmonary embolus approximately eight weeks after subtotal cystectomy.

Most patients were sent home 10 to 18 days after operation, while still draining urine suprapubically. As might be expected, the less bladder excised the sooner the patients were discharged from the hospital. The urethral catheter usually drained very little for the first week or two postoperatively. Most patients stopped draining urine from the suprapubic wound within three to five weeks after operation. Two patients having total cystectomy without ureteral transplantation drained urine slightly in excess for four months. All patients regenerated a new bladder which closed spontaneously.

One out of five patients (20%) developed some degree of ureterorenal reflux. This has on occasion been accompanied by minimal to moderate degrees of ureteral dilatation and hydronephrosis. The ureterectasis and pyelectasis usually decreased once definitive bladder size was attained (fig. 3). While ureterorenal reflux has been observed as part of this study, in eight years' experience with the procedure a clinical problem was presented in only one instance. That patient had severe, recurrent pyelonephritis which required vigorous antibiotic and chemotherapeutic drug therapy. It should also be reported that ureterorenal reflux can develop in a

Fig. 5.—Oblique cystogram taken one year after subtotal cystectomy demonstrating ureterorenal reflux; patient asymptomatic, urine sterile.

ureter which has not been disconnected and reanastomosed to the bladder. The significance of this observation is not clear but is under study at present.

Nocturia and diurnal urinary frequency were marked from one to two months postoperatively. At the end of four to six months none of the patients in the series had nocturia of more than two to three times each night. During the day, none voided more frequently than once every two to three hours. Cystographic appearance of the bladder demonstrates a viscus which is quite irregular (fig. 6). Cystograms taken at 4 months, 6 months, and 12 months show that there is an increase in bladder size from the fourth to the sixth month. Bladder capacity probably does not increase appreciably after 12 months. The mean bladder capacity for the patients studied ranged between 175 to 410 cc. of urine. The patient with 175 cc. of bladder urine capacity had total cystectomy with complete bladder regeneration. Only one patient in every 10 to 15 will have any residual urine. Residual urine has never been measured at more than 20 cc.

In all patients regeneration of the bladder occurred. In only one patient was the bladder capacity exceedingly small. This was in an individual 79 years of age. In a personal communication Lewis has noted also that patients of the very old age group regenerate with a small bladder capacity after a subtotal cystectomy.

The total number of patients followed for a full five-year postoperative period is too small to permit standard statistical comparison with other methods of management at this time. These results will be reportable later.

Fig. 6.—Cystogram taken one year after 90% subtotal cystectomy demonstrating irregularity of regenerated bladder; no residual urine.

It has been possible to obtain full thickness biopsy specimens of the regenerated bladder via the suprapubic route. Photomicrographs of the regenerated bladder demonstrate fibrous tissue interlaced with muscle fibers (fig. 7). These muscle fibers are not always continuous through the bladder wall. They originate as separate isolated muscle fibers in the fibrous bladder sheath (fig. 8). The presence of

Fig. 7.—Low magnification of full thickness biopsy of regenerated bladder wall; muscle and fibrous tissue present; epithelial surface at top, adventitial surface at bottom.

muscle in the regenerated bladder undoubtedly accounts for the notable lack of residual urine in all but a few of the patients studied. The fact that the muscle fibers initiate at individual sites within the fibrous tissue tends to support the view that muscle fibers are not an extension of ureteral or urethral musculature. Apparently the proximity of the urethra and ureters serves as an inductor phenomenon for development of muscle fibers from the totipotent mesenchymal-fibroblastic cell.

Patients who had extensive lesions of the bladder were also subject to subtotal cystectomy as a palliative procedure. It was found that eliminating the tumor mass and reanastomosing the ureter to the residual bladder made these patients considerably more comfortable. In addition, the patients had the

distinct advantage of being able to void via normal channels rather than using urinary or colostomy collection bags attached to the abdominal wall. In several patients the huge cancer had involved the bony walls of the pelvis and subtotal cystectomy could not be used. It is our opinion that very little could have been accomplished by any other type of surgical procedure with this type of advanced bladder cancer.

It was not hoped that any of the patients with advanced bladder cancer treated by total cystectomy would be cured of their disease. It should be added, however, that several of them are alive four, five, and seven years after subtotal cystectomy and are to date clinically free of cancer.

Fig. 8.—Regenerated bladder wall; arrows indicate isolated development or origin of separate muscle fibers. Masson stain (× 1,225).

Comment

The percentage of patients having bladder cancer which is potentially curable by transurethral or suprapubic segmental resection should be increased by use of subtotal cystectomy. Present statistics indicate that simple segmental resection effects a five-year survival rate equal to that of total cystectomy. It is certainly possible that those patients cured by total cystectomy could reasonably be expected to be cured by subtotal cystectomy. Of great importance to the patient is that with subtotal cystectomy the ureters are not transplaned elsewhere than to the bladder. As a consequence, these patients void via the urethra with full urinary control.

Subtotal cystectomy should be considered as a large segmental resection in which ureteral orifices are not spared at the expense of leaving cancer cells within the bladder. Subtotal cystectomy is a simple procedure which can be performed readily at any hospital by any urologist.

Many urologists do not like suprapubic segmental resection, as it is felt that manipulation of the tumor cells can disseminate these cells outside the bladder. This objection has been eliminated as patients in this series had preliminary transurethral resection of the entire lesion prior to subtotal cystectomy.

Patients with deeply infiltrating lesions at the vesical neck are probably not suitable candidates for subtotal cystectomy. These patients as well as those with proved multifocal cancer undoubtedly require total cystectomy. As described above, this does not imply that ureters must be diverted elsewhere.

While subtotal cystectomy is sometimes associated with prolonged suprapubic urinary drainage, this is no objection to the procedure. With cystectomy and transplantation of the ureters to an ileal pouch, there is permanent urinary drainage from an opening on the abdominal wall.

Urologists who perform lymphadenectomy at time of cystectomy will find some difficulty if subtotal cystectomy is used. In essence, the remaining bladder segment is in the way of the operator. Lymphadenectomy can be performed with subtotal cystectomy as completely and efficiently on the side containing the tumor, however, as when total cystectomy is employed.

The 20% incidence of ureterorenal reflux after subtotal cystectomy may appear as a major complication. It has not been so. We are well aware of the disadvantage of ureterorenal reflux, having been among the first to investigate and report on reflux after ureterointestinal anastomosis.[8] To date, the only adverse clinical effect of reflux we have seen is one patient with a severe unilateral pyelonephritis. This is considerably less than seen with any type of ureteral transplantation. Furthermore the incidence of radiographic renal and ureteral abnormalities is greater after any type of ureterointestinal anastomosis than the incidence of reflux in patients after subtotal cystectomy. By preservation of the normal voiding mechanism, subtotal cystectomy has advantages that do not require further discussion and outweigh any of the complications that have been encountered during eight years' experience with the procedure.

The use of subtotal cystectomy in patients with far-advanced bladder cancer appears to be worthwhile as a palliative procedure, as it removes the large irritating and often bleeding mass. As the procedure permits reimplantation of an involved ureter to a normal segment of the bladder, these patients void with normal urinary control. In most

patients with far-advanced bladder cancer, when the procedure can be used at all, it is preferred by us to any other we have previously employed.

Summary

Subtotal cystectomy in treatment of bladder cancer of superficial or deep infiltrating types is presented as a substitute for other surgical methods now universally employed. Bladder regeneration after subtotal and total cystectomy indicates that muscle formation originates from the totipotent mesenchymal cell and not as direct extension from ureteral or urethral musculature.

3800 Reservoir Rd. N. W. (7) (Dr. Baker).

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PREVENTIVE AND AVIATION MEDICINE IN PRIVATE PRACTICE

Russell J. Vastine Jr., M.D., Niles, Mich.

It is possible to devote a private practice to preventive and aviation medicine. Its objective is to supply people with a particular type of health service that will enhance well-being and prolong life. Its essential features are thorough examinations and subsequent instruction. Its application is especially natural in connection with aviation, for there is evidence that examinations of pilots have often been perfunctory and that there are ambulatory persons who should not fly. The program of history-taking, physical examination, and laboratory tests here outlined has been found efficient. Such a survey should be an annual affair for both private and airline pilots, regardless of rating. It is easily adapted to all persons interested in maintaining their health.

Most authors have written that the private practice of preventive and aviation medicine is not feasible. With this I disagree. However, I am taking a different approach to the subject than most persons. We must first come to an understanding of definitions and responsibilities of a private practice of this sort.

It is impossible for one to establish a practice to supplant the public health officer. It is impossible to furnish epidemiologic studies for communities and to supply diagnostic laboratory studies, such as a good public health office does. It is, however, possible to supply individuals with a particular type of health service that will greatly enhance their well-being and will, in the long run, statistically increase their longevity. This, then, is the objective of a private practice devoted to preventive and aviation medicine.

Fitness in Flying

Aviation medicine is a special branch of preventive medicine. Just as the pilot practices preventive maintenance for his airplane, so must he practice preventive maintenance for himself. As you know, the pilot is required by law to undergo periodic medical examinations in order to maintain his license. It is in this field of medical endeavor that the medical profession has failed miserably. The caliber of examination to which these persons have been exposed is outrageous. Medical certificates

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have been issued with only a minimal examination, sometimes with no examination at all. We have insisted on periodic examinations for safety reasons and then have failed to perform them satisfactorily. No wonder, then, the pilot feels distrust for those of us who wish to maintain air safety. No wonder, then, the pilot feels that the medical standards are useless. Physical fitness is important to flying safety, but how can this be proved when we have such poor medical supervision of flying personnel?

To cite an example of the importance of physical fitness to flying safety, I recall a pilot I examined for an airline transport pilot's rating. Using the Civil Aeronautics Administration's chart for testing near vision, I found this man could not read the bottom paragraph with either eye and could only barely make it out with binocular vision. His chief complaint was with night vision. He had trouble reading his maps at night because he had to hold them close to his face to protect the night vision of his co-pilot from the flashlight he used. This man admitted that it had been at least four years since he had been able to read this bottom line. He had been examined at six-month intervals during this period and had never been told his eyes needed correcting lenses, and his medical certificate had never been marked with a limitation. This visual defect was severe enough to cause this man to refrain from filing flight plans unless his radio had been set previously, because he could not read the dials. Here is an excellent pilot endangering himself and all those in the airplane because of a physical defect. His new glasses have increased flying safety for all concerned.

Annual Health Survey

Since we have already stated the objective of a private practice devoted to preventive and aviation medicine and since we have discovered that aviation medicine is preventive medicine, let us set about outlining the responsibilities of this type of practice. Probably the most outstanding service to be offered by this type of practice, and the one in which there is the greatest need for action soon, is the periodic examination. My personal opinion is that an annual examination is adequate unless some defect be found that would dictate more frequent ones. I would prefer to call this examination an annual health survey. I am sure that no one in his own practice would ask a patient to return for such a survey more often than once a year. Pilots are no different. This survey should be an annual affair for all pilots, regardless of rating. The private pilot uses the same air space as the airline pilot and is subject to the same stresses of flying and living. While cost is a factor in the survey I am about to recommend, it is no more costly than seven hours' rental of a Piper Cub or a 50-hour inspection of an airplane.

A complete history of present complaints, along with a searching review of symptoms by systems, should be the first step in the annual health survey. This should be taken by the examining physician for what appear to be obvious reasons, but perhaps some of them should be stated. The examiner will acquaint himself with the type of person he is examining and will gain insight into the complaints the patient has. Most of all, he will be able, if he knows how to fly himself, to get a fair picture of the type of pilot he is examining. This latter point is where we all fall down. Industries using aircraft, as well as the airlines, are interested in finding a simple means of discovering if a pilot will be a potential cause of accident before they hire him. By making a personality analysis and honestly checking it with some one who has flown with the pilot, we will some day be able to put on paper what we look for and provide a long-needed answer. This I have done in my practice. I have been lucky in my decisions. The reason for this is that I am a pilot myself and have a pilot's point of view. If you have never been in a tight squeeze in an airplane or never have been faced with making rapid decisions while in an airplane, it is sometimes difficult to understand what the pilot is telling you. A few hours of flight time is not the answer. The taking of a thorough personal and family history is also important in this phase of the annual health survey.

The physical examination should be done with care and precision, noting any and all defects, no matter how slight. This will some day pay excellent dividends when the examinations are reviewed with an eye toward determining the natural history of some particular disease. We do not know now what may be important later, so we must not omit anything. Included in the physical examination should be a pure-tone audiometry. Many early hearing losses, particularly in those persons who are exposed to noise, will be found only if this is done. No physical examination is complete without a sigmoidoscopy. This can easily be done without preparation on the part of the patient. One of the disposable enemas, given when the history has been completed and before the physical examination is begun, will clean the distal portion of the intestine nicely so that the scope can be passed to 25 cm. with ease. Only rarely does the enema need to be repeated. This method is acceptable to the patient. I have not had to use air insufflation in a single case. More complaints have been registered during the rectal examination than during the sigmoidoscopy.

If at all possible, prostatic secretion should be obtained for examination under the microscope. I have been amazed at the number of cases of symptomless, mild prostatic disease I have found that respond well to sitz baths.

Examination of the eyes should include testing of both distant and near visual acuity and visual fields. Early glaucoma can be helped. While tonometry is ideal, I have not yet become convinced that it ought to be made a part of routine procedure.

In order to complete the annual health survey, certain ancillary studies should be done. These include an electrocardiogram, a two-meter postero-anterior chest x-ray, a complete urinalysis, a complete blood cell count (or a hematocrit determination and differential count), and determination of sedimentation rate and nonfasting blood sugar, blood urea nitrogen, and blood cholesterol levels. Serologic examination is also done and, for the patient's own satisfaction, blood type and Rh-factor determinations. Most of these studies need no discussion as to their usefulness, but perhaps a word should be said about the cholesterol level determination. This was chosen for two reasons, the first of which is more of a research problem. The ever-increasing discussion of cholesterol and its relation to heart disease and arteriosclerosis makes it worthwhile to make routine determinations to perhaps help in the study of the natural history of disease. The second reason for this choice is that it offers a simple means of roughly measuring thyroid function. My patients come to me on a fly-in basis, and it is not feasible to examine these persons in a fasting state so that the basal metabolic rate can be determined. Nor is it convenient to draw additional blood in chemically clean glassware for protein-bound iodine determination. This would also increase the cost of the annual health survey. Thus, the blood cholesterol level is determined. I have stated that these blood specimens are drawn on the nonfasting patient. This, I feel, is a truer picture of the function of the organs involved in these studies than is the fasting state. As a part of the history interview, I review the diet for the past 24 hours. I note the time of the last meal and the time the blood was drawn. Some day I will be able to review these examinations, calculate roughly the amount of food intake, and establish normals for the nonfasting state. It may have many other ramifications that are not now readily noticeable.

The annual health survey I have just reviewed consumes between two and three hours. The cost at present has been set at $70. For what is done, I feel this is a realistic fee. One will never get rich doing this sort of thing, but he won't starve. The x-rays are read by a radiologist, and the laboratory work, except for the blood cell count and urinalysis, is done in a recognized laboratory. The patient is getting a rather extensive review of his health at a reasonable cost. By performing these annually, an excellent case study is established so that even the slightest change may be readily found. This then affords an opportunity for diagnosis of symptomless disease and thereby prevention of serious illness.

Further Responsibilities of Aviation Medicine

This is not complete for the prevention of disease because we are not yet able to follow the natural history of illness, but I sincerely feel that what I am doing will some day offer some of the answers. An objective is also to make flying safer and prolong the productive life of the pilot.

Another responsibility of this type of practice is to the passenger. Regardless of the stand of the airlines, there are certain ambulatory persons who should not fly. The practitioner of aviation medicine must be aware of these ailments and advise the pilot and the passenger of limitations to be observed in flight. Corporate flying increases the exposure of this type of person to the effects of flying without supervision. Very few companies have any rules regarding restriction of flight for their personnel. Advice should also be available concerning prevention and treatment of the diseases incident to flight, such as aerotitis and aerosinusitis. The use of a nasal spray, at the proper time, will reduce pain and lost work.

The physician in this kind of practice should also be available for assistance in establishing retirement and temporary grounding policies that will add to the peace of mind of the pilot. This will give him more mental space for flying. The physician should take an active part in the training of the pilot. He should be called on to teach first aid and to give instruction in the medical aspects of flight. Demonstrations of the effects of oxygen want are more valuable than all the words one can command.

Selection of aircraft and revision of present aircraft always present problems. There are few people who can do it well, but the physician can help in the fields of passenger comfort, cockpit engineering, cabin ventilation, availability of oxygen equipment, and its selection, if its need is anticipated. Also, advice concerning safety features should be forthcoming.

Conclusions

There is great opportunity in this field of aviation medicine for research on an individual basis in matters concerning aviation as well as in matters pertaining to the prevention of disease. The more of us who will participate in this type of program, the more facts will we accumulate to aid all doctors in their effort to control disease.

While this practice is intended to be devoted to the pilot, it is easily adapted to all persons who are interested in the maintenance of their health. Until aviation personnel can be ethically told and can accept what I am trying to do, my income is dependent on nonflying persons.

2026 Lake St.

TWENTY-YEAR STUDY OF PHYSIOLOGICAL MEASUREMENTS IN ONE HUNDRED SENIOR AIRLINE PILOTS

George J. Kidera, M.D., Chicago

Unusually complete sets of physical and laboratory measurements were obtained from 100 men who had been participating actively in the piloting of commercial aircraft for 20 years. This group underwent a rigorous process of selection not only at the beginning but also throughout the duration of their careers as fliers. The average age was 30.5 years at the beginning and 50.5 years at the termination of the study. The most striking changes were a gain of 5.4 kg. (12 lb.) above the initial mean weight of 71.4 kg. (157.5 lb.), a decline of 969 cc. from the initial mean vital capacity of 4,962 cc., and an increase of 5.0 and 4.5 cm., respectively, in the girth of the abdomen and unexpanded chest. Blood pressure and heart rate remained remarkably constant, but impairment of near vision was striking, since 91 men required presbyopic correction by 1957. Audiometric losses were found, amounting to 2.85% for the right ear and 4.6% for the left, but these were roughly equal to those found in the general population. There was no evidence, in this study, of occupational predilection for any particular physical disorder.

For several years physicians of commercial airlines who perform periodic physical examinations on flight personnel have been requested by various groups studying aging to report their findings on pilots in order to document any particular premature physiological deterioration in this group. The airline pilot was recommended for this study for several reasons. First, the airline's type of flight physical examination is complete, consisting of a history and careful examination. Particular reference is made to the special senses and laboratory tests, such as routine chest x-ray, routine electrocardiograms, stress electrocardiograms, sedimentation rate, and complete blood cell counts.

If a deviation from normal is noted in any phase of examination, the airline medical department's approach is slightly different than that in private practice. It behooves the airline to establish a definitive diagnosis and assess and evaluate completely the deviation, regardless of its immediate clinical significance. An example of this would be the detection of minor T-wave changes in a pilot who previously had normal electrocardiographic tracings. In private practice one might recommend further studies, such as thyroid function, stress electrocardiogram, total blood fat determination, and ballistocardiogram. The private patient may not be disposed to undergo such an exhaustive study. When such a deviation is detected in a commercial airline pilot, it is absolutely necessary that the condition be assessed and no avenue of study is left unexplored, in view of the responsibilities incident to the pilot's profession.

Another reason for selecting airline pilots for this study is the fact that these men are periodically examined by the same group of full-time company doctors. Laboratory procedures, even though a 20-year span is covered by this study, have been performed by not more than five different laboratory technicians. This consistency of professional personnel tends to result in more accurate study data than if results from many physicians, clinics, and laboratories are reviewed.

The question whether irregular hours and hypoxia might be factors in deterioration could also be studied by evaluating the physical condition of airline pilots, since many of the senior captains flew in the days prior to pressurization of aircraft and were exposed regularly to altitudes of 10,000 to 14,000 ft. With the advent of pressurized aircraft, this exposure is limited to usually less than 8,000 and more frequently to 5,000 or 6,000 ft.

Medical Director, United Air Lines, Inc.

Read before the Joint Meeting of the Section on Preventive Medicine and the Aero Medical Association at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Materials and Methods

A study of airline pilots does not lend itself to a study on aging per se, since the age group represented cannot be considered aged and there are not enough commercial airline pilots over 50 years of age to give valid statistical criteria. Consequently, this report is concerned with what could be referred to as a middle-aged group. These records are a continuous account of the physical status of these men from the time of their preemployment examination to their current company-prescribed physical examination. These pilots not only receive a thorough annual physical assessment but also must be given medical clearance for resumption of flight duties after any illness or injury.

Flight personnel are also encouraged to consult the physicians not only on personal problems but also on any medical problems relating to their families. This gives the flight surgeons an opportunity to visit and consult with the pilots four to five times per year. One of the most important factors in attaining good liaison with the flight personnel is the position of the medical depart-

ment in the company's organization. The United Air Lines medical department does not report to any other administration or agency. All medical records, reports of consultations, and results of examinations are confidential and are made available only to the pilot. Management is advised that an individual is physically qualified or disqualified for further flying, and no data are furnished to anyone unless specifically requested in writing by the pilot. This doctor-patient relationship is of utmost importance in building up free communication between the flight surgeon and the pilot.

At the initiation of this study in 1937, the ages of these 100 airline pilots ranged from 25 to 39 years, with an average age of 30.5. In 1957, the average age was 50.5 years and the range 45 to 59.

Results

A consideration of actual findings of those factors which lend themselves to a quantitative comparison follows.

In 1937, all 100 pilots had distant vision of 20/20 or better in each eye. By 1957, 20 needed glasses to bring their vision to 20/20. The poorest vision in this group was 20/50 for the right eye and 20/67 for the left. Dimond's report [1] of a small series of airline pilots is of interest. In those with a preemployment cycloplegia of +0.25 to −0.25 D., the defect in some remained stabilized but there was a physiological and developmental trend toward myopia. With a preemployment cycloplegic refraction of +0.675 D. or more, most pilots will continue to have hypermetropia (hyperopia) with 20/20 vision throughout their anticipated long span of duty. Consequently, 20/20 vision and a manifest or homatropine-produced hypermetropic reserve of +0.50 D. or more in the early to mid-20's is desirable in the prospective airline pilot.

Near vision for the group was calculated as 1 on the Jaeger system in 1937. By 1957, 91% required presbyopic correction (at an average age of 44.5 years). Other eye findings are shown in table 1.

TABLE 1.—*Average Eye Findings in 100 Commercial Airline Pilots Over Twenty Years*

	1937	1957
Depth perception, mm. (Howard-Dohlman)	11.10	12.90
Abduction, D.*	6.11	5.65
Adduction, D.	13.80	13.05
Esophoria (20 ft.), D.	1.48	0.76
Exophoria (20 ft.), D.	0.42	0.29

* Diopters.

In the general population one sees a tendency toward an increase in adduction in the development of exophoria, especially with accommodative problems. This was not noted in the pilot group, since they were given corrective lenses for accommodative problems early. The average depth perception was essentially unchanged, as would be expected since depth perception is primarily a product of good binocular vision.

In 1937, five had hearing less than 20/20 when using the spoken voice test. This ranged from 15/20 to 18/20. In 1957, the lowest value was 5/20 hearing for the spoken voice in one ear. In 1937, the voice-range audiometric findings were practically normal, but some high-tone loss was noted. The average loss was 12% for the right ear and 13.8% for the left ear. In 1957, 61 showed a loss for the

TABLE 2.—*Average Blood Findings in 100 Commercial Airline Pilots Over Twenty Years*

	1937	1957
Red blood cell count, cu. mm.	5,402,000	5,315,400
Hemoglobin level, Gm. % (Sahli)	15.35	15.82
White blood cell count, cu. mm.	10,450	9,500
Sedimentation rate, mm./hr. (Cutler)	7.9	6.8

frequencies above 4,000 cps, 16% for the right ear and 17% for the left ear. In 1957, with use of the method for calculating percentage hearing loss recommended by the American Medical Association Committee on Medical Rating of Physical Impairment, a loss in the 500-to-4,000-cps range was found of 2.85% for the right ear and 4.6% for the left ear. These audiometric losses compare favorably with those of ground personnel of similar ages.

Height averaged 69¾ in. (177 cm.), and there was no significant change over the 20-year period. In reviewing the weight gain it was anticipated that a rather sizable increase in weight over the 20 years would be found. This was not the case. Weight in 1937 averaged 157½ lb. (71.4 kg.), with a variation between 211 and 127 lb. (96.2 and 57.6 kg.), while in 1957 the average was 169½ lb. (76.9 kg.). The heaviest man weighed 221 lb. (111.2 kg.) and the lightest 136 lb. (61.7 kg.). An average weight gain of 12 lb. (5.4 kg.) during a 20-year span was considered excellent. This is further emphasized in the light of a report by Captain Huber of the U. S. Navy (Huber studied a group of Navy pilots and found an average weight gain of 29 lb. [13.2 kg.] per man over a 10-year period). Unexpanded chest measurement in 1937 averaged 35.25 in. and the abdominal measurement 31.43 in. Twenty years later the values were 37.04 and 33.4 in. respectively.

Pulse rate, blood pressure, and vital capacity were periodically determined, and in 1937 and 1957 the average compared as follows: pulse rate, 65.9 and 65.5 per minute; blood pressure, 114/72 and 115/78 mm. Hg (ranges, 96/56 to 154/78 in 1937 and 98/58 to 158/84 in 1957); and vital capacity, 4,962 cc. and 3,993 cc. (ranges, 3,100 to 5,900 in 1937 and 3,000 to 4,850 in 1957). The highest recorded blood pressure was 158/84 mm. Hg; this occurred on a single reading, in 1957, in the same man who, in 1937, had the highest reading, 154/78 mm. Hg. Similarly, the man who, in 1937, had the lowest blood pressure recording, 96/56 mm. Hg, also had the lowest reading in 1957, 98/58 mm. Hg. The vital capacity from 1937 to 1950 was measured by a water spirometer. Subsequent to 1950, the Propper compact spirometer has been used.

The blood findings at every physical examination proved to be extremely consistent. These are summarized in table 2.

In an attempt to evaluate physical status, absenteeism over the 20-year period was studied in this group of pilots. There were 8,267 days lost, which amounts to slightly over 4 days per year per man. The nature of the illness responsible for absenteeism is strikingly similar to that reported by industry in general, and it compared almost to the number for a similar group of ground personnel within the company, with one exception. Upper respiratory infections accounted for approximately 40% of the days lost. The next highest percentage, and this is the exception, was absence due to trauma. This acounted for almost 20% of the pilots' absenteeism. Traumatic injuries resulted in 1,893 days lost. While this is high in relation to illness, it is of interest to note that the traumatic injuries were primarily incurred in recreational activities, such as baseball, skiing, working with power tools, and other "do-it-yourself" programs. The pilot group is usually an athletic group with considerable time for hobbies and diversion, which apparently exposes them to a greater incidence of trauma. The remainder of the causes of absenteeism ranged through all of the illnesses and injuries to which man is heir. Other than traumatic injuries, there was no prevalence of any diseases as compared to nonflying personnel.

Summary

Physical and laboratory findings in 100 senior airline captains over a 20-year period were studied. The homeostasis presented by this group was impressive. In spite of 20 years of their active participation in piloting commercial aircraft, there was no evidence of premature deterioration or predilection to any particular medical or surgical condition.

5959 S. Cicero Ave. (38).

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ROLE OF THE HUMAN FACTORS BRANCH AT THE AIR FORCE FLIGHT TEST CENTER

Lieut. Col. Burt Rowen (MC), U. S. A. F.

The Air Force Flight Test Center (AFFTC) is located in the Mojave Desert, approximately 75 nautical miles northeast of Los Angeles, and occupies approximately 300,000 acres of land. The physical location of the center is built around the 65 square miles of Rogers Dry Lake, and it is estimated that this concrete-hard lake bed, which serves as a natural emergency landing field, has saved over 630 million dollars in hardware alone since April, 1946. Naturally, no estimate is placed on the lives saved. The AFFTC includes a rocket engine test facility, a high-speed sled track, a precision bombing range, an all-altitude speed course, the U. S. A. F. Experimental Flight Test Pilot School, and the high-speed flight station of the National Advisory Committee for Aeronautics.

Since 1949, U. S. A. F. flight testing has been divided into eight phases by Air Force Regulation 80-14. These divisions are as follows: phase 1, air

Chief, Human Factors Branch, Directorate of Flight Test, Air Force Flight Test Center, Edwards Air Force Base, California.

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The mission of the Human Factors Branch at the Air Force Flight Test Center is to study the design and functional characteristics of research aircraft and weapons systems as related to human capabilities, to evaluate the man-machine relationship, and to recommend appropriate changes. Today almost every contractor in the aircraft industry has a human factors or a human engineering staff. It is gratifying to realize that there is a large human engineering work force-in-being dedicated to tailoring an aircraft to suit the human operator. Everyone concerned with instrumenting, equipping, and modifying cockpit arrangements of piloted aircraft has realized the necessity of relieving the crew member of as many details of aircraft operation as possible, if missions are to be successful.

worthiness; 2, contractor compliance; 3, design refinement; 4, performance stability; 5, all-weather; 6, functional development; 7, employment suitability; and 8, unit operational employment.

In the near future a revised Air Force Regulation 80-14 will change the U. S. A. F. flight testing concept. The new regulation provides for earlier and increased participation by the using commands in the testing of new systems planned for the U. S. A. F. inventory. The purpose of this revision is to assure the earliest possible introduction of proved systems into the inventory and minimize the impact on the combat capability of using commands.

The new test concept calls for integrated test programs with provisions for participation of the using commands and other interested agencies in a combined test force. It will establish the following three general categories of testing: 1. Subsystem development and evaluation. This will correspond to phases 1, 2, and 3. 2. System development and evaluation. This will correspond to phases 4, 5, and 6. 3. System operational evaluation. This will correspond to phases 7 and 8. Pending formal publication of the revised regulation, all commands are directed to cooperate in initiating action for execution of test programs on new systems in conformance with this policy.

Mission of the Human Factors Branch

The mission of the Human Factors Branch at the AFFTC is to study the design and functional characteristics of aircraft weapon systems as related to human capabilities; to evaluate the man-machine relationship; and to recommend appropriate changes. The Human Factors Branch is a part of the Flight Test Engineering Division. This is one of the four divisions of the Directorate of Flight Test, the others being Flight Test Operations Division, Technical Services Division, and Technical Facilities Division. The Technical Services Division includes the Power Plant Branch, Armament Branch, Photography Branch, and the Experimental Track Branch. The Technical Facilities Division includes the Instrumentation Branch, Data Reduction Branch, Telemetering Branch, and the Space Positioning Branch.

Air Force human factors personnel participate with contractor human factors groups and preliminary design engineers during planning and preliminary design of a weapon system or research vehicle. Recommendations for changing features of the system which affect the human operator are submitted at this early stage of development whenever or wherever practicable. Air Force and contractor personnel maintain close liaison with each other during this stage of development. It is of interest to note that prior to an aircraft's first flight and subsequent entry into the formal U. S. A. F. test program many inspections are accomplished. Experts in the field of power plants, airframes, fuels, oxygen, hydraulics, electronics, armament, cockpit layout, escape systems, and others all attend these formal inspections. At these meetings written requests for alterations (RFA) are tied to the various components which are in need of modification. All these items are discussed and categorized, and eventually the first model or prototype is flown. In spite of all this prior effort, a new series of "squawks" or deficiencies become evident as soon as the aircraft begins to fly.

During phase 2, 4, and 6 testing, human factors project officers are a part of the project control team at Edwards Air Force Base. They work in close cooperation with project engineers of the Flight Test Engineering Division and with project pilots of the Flight Test Operations Division. They depend to a large extent on pilot comments for single-place aircraft and pilot comments plus flight participation in multiplace aircraft. The human factors officers examine and study all human factors problems in the weapon system appearing during phase testing. The following areas are examined: armament, auxiliary equipment, controls, communication, crew welfare and comfort, emergency escape, emergency systems, environment, human performance, instruments and indicators, lighting, maintenance problems, mobility, noise, oxygen system, personal equipment and aircraft compatibility, pressurization system, pressure suits and allied equipment, psychological factors, safety, seating configuration, training, and visibility.

Human factors comments become an integral part of the technical reports that are published at the conclusion of phases 2, 4, and 6. The technical report completely describes the operational characteristics of the aircraft, lists discrepancies, and includes recommended modifications for improvement of unsatisfactory systems.

ARDC Manual 80-1, the Handbook of Instructions for Aircraft Designers (HIAD), is used as a guide by the contractors in designing and equipping a new aircraft that enters the test inventory. This periodically revised document was originally issued in July, 1955. The instructions in the HIAD are of a general nature, and the contractors are permitted a certain freedom in complying with these instructions. The HIAD has references to military specifications for detailed descriptions of special installations. Most of the recommendations submitted by the Human Factors Branch concern details of installation, operation, or maintenance, which are improvements of a contractor's installation from a crew member's operational viewpoint.

There are exceptions to this optimal situation in the procurement of aircraft. One outstanding example is the KC-135 procurement without ejection seats even though the HIAD requires them. The KC-135 is the Air Force fuel-carrying version of the

passenger-carrying Boeing 707. In this particular case, the military tanker is not equipped with ejection seats. The requirement of early delivery took precedence over a jet tanker ejection seat development program.

Where appropriate HIAD instructions followed by a contractor are still found to be unsatisfactory from a flight test crew member's viewpoint, a report of the situation is made. After coordination with local technical or factory representatives, project pilot, and project engineer, recommendations are forwarded to the Commander, Wright Air Development Center, Attention WCXH, Wright-Patterson Air Force Base, Ohio, describing the preferable system or installation so that the Handbook of Instructions for Aircraft Designers may be correspondingly altered.

Effects of Recommendations and Reports

It has been gratifying to see newer aircraft appearing at the AFFTC which incorporate the majority of recommendations submitted in previous technical reports. The F-100 series, the F-105, and F-106 are excellent examples of contractor follow-up aimed at making the aircraft easier for the pilot to operate. During the past four to five years the aircraft industry has realized the increasing requirement for human factors effort within their own production capability. Today almost every contractor in the aircraft industry has a human factors or a human engineering staff. These staffs vary in size, commensurate with the production capability of the individual corporation, and are composed of a variety of professional personnel in the fields of physiology, psychology, medicine, engineering, and the basic sciences. The Edwards Air Force Base Human Factors Branch is of a similar organization. It is gratifying to realize that there is a large human engineering work force-in-being dedicated to tailoring an aircraft to suit the human operator. Everyone concerned with instrumenting, equipping, and modifying cockpit arrangements of piloted aircraft has realized the necessity of relieving the crew member of as many details of aircraft operation as possible, if missions are to be successful. To evaluate our own ability to identify potential problem areas in test aircraft, personnel of the Human Factors Branch visit the using agencies and discuss current operational problems. By means of a questionnaire and informal pilot interviews, a comparison can be made between problems appearing during flight test evaluation and subsequent tactical employment. To date, this has been done on the F-100C, F-101A, F-102A, and C-133A. Results indicate a reliable identification of problem areas during the flight test program. In the maintenance field, a survey of the fire control, engine, electrical, and weapons repairmen was made at Bergstrom Air Force Base, where the F-101A is being flown operationally. All maintenance personnel were asked to rate their particular system numerically regarding accessibility, simplicity, adequacy of tools, reliability of components, and adequacy of ground handling equipment. When these numerical ratings were compared with similar maintenance ratings performance at Edwards Air Force Base while the aircraft was under flight test evaluation, a very close correlation was observed. This would indicate a reliable means of identifying maintenance problem areas which using commands would necessarily want covered by additional training. In some instances unanticipated problems occur in tactical employment because of newer equipment supplied for production of aircraft previously unavailable during the earlier flight test evaluation. A typical example of this is a newer oxygen system supplied for production of F-102A aircraft. This particular oxygen system was not available during the flight test program of the F-102A aircraft.

Aeronautical Medical Support Mission

An interesting aeronautical medical support mission presents itself in the field of research aircraft. For approximately 10 years, aeronautical engineers have been recording in-flight data from instrumented aircraft on ground read-out indicators through telemetry. In the past, when a research aircraft arrived at its flight phase of development and was put in flight, the pilot's physiological status was never recorded during flight. This was the situation during the X-2 program. During the flight phase of the X-15 aircraft, physiological data will be telemetered so that a flight surgeon observing the ground read-out can tell when the pilot is approaching the limit of his physiological tolerance. This will quantitatively identify the most stressful portion of a particular mission profile.

The full pressure suits to be worn during the X-15 program were specifically designed with 12 electrical contact points to facilitate the necessary connections between the telemetering sensers and transmitters.

With current techniques of closed-loop dynamic simulation, it is now possible to record additional physiological data during simulated flight trajectories. During the dynamic simulation at the Naval Air Development Center, Aviation Medical Acceleration Laboratory, Johnsville, Pa., electrocardiographic data were recorded but not telemetered.

Before the first flight date of the X-15 in 1959, pilots' physiological data will be telemetered to ground recording stations to evaluate and prove this technique, with use of a TF-102 which has been specifically assigned the Air Force Flight Test Center for this project. Physiological data will be recorded at Edwards Air Force Base, Calif., by means of currently operational National Advisory Committee for Aeronautics High-Speed Flight Station and U. S. A. F. telemetering receivers.

Items such as (1) cockpit pressure, suit pressure differential, (2) helmet pressure, suit pressure differential, (3) pilot's body surface temperature, and (4) electrocardiographic data will be monitored by a flight surgeon at the ground receiving station during flight. The body surface temperature will be correlated with recorded cockpit temperature. This is an extension of the electrocardiographic recording system monitored by a physician during the centrifuge simulation program at the Naval Air Development Center at Johnsville, Pa. This system has a growth potential for additional data recording and is currently being developed by the contractor. For certain missions, specific data can be collected, permitting a flexibility of operation. The objectives of the TF-102 program at the Air Force Flight Test Center are (1) training and familiarization for X-15 pilots; (2) physiological instrumentation research and development and establishment of criteria for future crew selection; (3) standardization of MC-2 suits; (4) product improvement of MC-2 suit assembly for future weapon systems; and (5) operational capability of the MC-2 suit. To date, approximately 10 hours of actual flight time has been accumulated on the MC-2 suit assembly. The transducers for these measurements are all miniaturized and will not hinder pilot performance in any way. The flat electrocardiographic pick-ups, for example, are approximately the size of small dental x-ray films about 1.25 in. square.

Another interesting aspect of physiological monitoring of pilots associated with the X-15 program is the whole-body radiation level. The University of California operates a whole-body radiation counter for the Los Alamos Scientific Laboratory about 70 miles north of Albuquerque, N. Mex., in the Los Alamos airspace prohibited area. This device is shielded by 20 tons of lead and has been used as an investigative tool in measuring whole-body radiation levels of over 3,000 persons. This gamma counter measures radioactive potassium (K^{40}), a constituent of muscle tissue, and identifies radioactivity as so many counts per second. Preflight base-line K^{40} activity will be obtained from pilots in this program and later correlated with postflight levels. The anticipated increased activity represents a quantitative increment of cosmic radiation effects which will be available for the first time from a human subject flying a research aircraft. This program, with use of the only known whole-body radiation counter, is easy to implement. The only portion that needs to be hurried is the trip back to Los Alamos Scientific Laboratory after landing from a high altitude flight. Since the induced whole-body radioactivity of K^{40} has a half-life of 12.8 hours, the pilot's postflight radioactivity therefore returns to normal in about three days. The technique of performing the whole-body count is very simple, requiring only three minutes, and does not involve the use of drugs. The Los Alamos Scientific Laboratory will obtain a newer whole-body radiation counter for transportation to and installation at the Air Force Flight Test Center.

The Air Force Cambridge Research Center, on inquiry, has expressed a position of interest and complete cooperation regarding assistance in obtaining quantitative data of cosmic-ray activity on the surface of the X-15 itself. These results, compared with the pilot's whole-body radiation activity, should be extremely informative regarding the relation between pilot and aircraft exposure to cosmic-ray activity. The initial proposals include (1) an abrasion detector to measure crater erosion, (2) cosmic radiation by emulsion, and (3) micrometeorite detection.

This, briefly, is the Human Factors or Aero Medical support program for the X-15. The over-all objectives are to obtain quantitative physiological data and to make the pilot's actual flight task a realistic continuation of previous experience and training. The procedures for accomplishing these goals are in existence today; they need only further refinement in an operational aircraft to make their use a reality when the X-15 begins its scheduled flight program.

Conclusions

In closing I think it appropriate to quote from the Handbook of Instructions for Aircraft Designers:

> Investigations in aviation medicine have shown the importance of human capabilities and limitations in aircraft design. Investigations in aviation medicine have augmented knowledge and continue to disclose supplementary data on the physiological and psychological limitations of the human system. As aircraft become more complex, and as their performance characteristics make greater demands on the physical and mental capabilities of the crew, the designer must recognize and cater to these definite limits lest the best conceived aircraft make inordinate demands on the flyer from mechanical, aerodynamic, or tactical standpoints. Further, although the aircraft may operate within the range of human capabilities, a lack of proper consideration for the flyer's comfort and safety, and therefore his efficiency, will result in unwarranted reduction in the effectiveness of the aircraft. Attention to crew safety, comfort, and efficiency at early stages in the design of an aircraft often results in satisfactory provisions with little or no performance penalty.

As members of the Air Force flight test team, those of us engaged in human factors efforts feel that we are contributing to safety, comfort, and efficiency of future manned weapon system and manned research aircraft.

MEDICAL CONSIDERATIONS OF EXPOSURE TO MICROWAVES (RADAR)

Charles I. Barron, M.D.
and
Albert A. Baraff, M.D., Burbank, Calif.

Apprehension over the possibility of injury to man by microwaves is based largely on the fact that sufficiently intense and prolonged radiation of this frequency has caused severe injuries to experimental animals. Several hundred workers who have been occupied about radar installations or have been exposed to radar beams have therefore been observed in a comprehensive medical surveillance program. This has been in progress for four years. The initial study was a comparison of 88 nonexposed persons with 226 radar-exposed employees, some of whom had worked with radar as long as 13 years. No acute, transient, or cumulative physiological or pathological changes attributable to microwaves have been revealed by this study in people working with high-power radar transmitters and frequently exposed to their output. These subjects are free to heed the warning sensation of heat and are advised to avoid exposure to any firing beam when in a zone defined by a minimum power density of 0.0131 watts per square centimeter. Since the development of increasingly high-powered transmitters is to be anticipated, the need for more precise and refined statements of human tolerance is evident.

Considerable interest in the biological aspects of exposure to radar beams has been generated during the past year by widespread publicity of an alleged case of human death occurring after a brief exposure to an unknown quantum of microwaves.[1] The incident served to direct attention to this relatively new agent, and questions naturally arose concerning the extent of the hazard, if any, to persons working with radar transmitters and to those who might be exposed in some manner to the energized beam. Many of these questions have subsequently been answered, and much needed research is being conducted by military and civilian agencies to more closely explore the multifaceted disciplines associated with this complex problem. Unfortunately, these less sensational but more scientifically conducted efforts have received little recognition or dissemination beyond the scientific world.

It is not generally known that apprehension over the biological potentials of microwaves dates back to the early days of World War II, when Daily[2] performed his original studies on U. S. Navy personnel engaged in the operation and testing of relatively low-powered radars. Although this study revealed no evidence of radar-induced pathology in human beings, numerous reports have since appeared indicating that tissue injury and animal death can occur under certain experimental conditions. These studies indicate that cataracts, corneal opacities, testicular degeneration, and hemorrhagic phenomena have been induced in anesthetized, small, furry, test animals by exposure to microwaves in the frequency range of 2,800 to 9,000 megacycles for various time exposures. Boysen,[3] using a transmitter with a frequency of 300 megacycles, exposed rabbits in a wave guide and produced damage to the central nervous system, degenerative changes in the kidneys, heart, liver, and gastrointestinal tract, and hemorrhagic changes in the respiratory tree. The power density measured in the wave guide was in excess of 0.1 watts per square centimeter. The animals were exposed for periods of 7 to 10 minutes, and all whose rectal temperatures exceeded 44.5 C (112.1 F) died. Boysen was of the opinion that the pathology and death were causally related to the hyperthermia.

Because of these rather startling findings and the apprehension engendered by their publication in scientific journals, the medical department of the airframe manufacturer, Lockheed Aircraft Corporation, coincidentally installing, testing, and servicing the most powerful airborne transmitters, early in 1954 instituted a comprehensive medical surveillance program for its several hundred employees working with radar or those who might be exposed to the energized beam. This program has now been in progress for four years and constitutes one of the longest continuous medical surveys of radar-exposed personnel in the United States. It is because of this that we believe the results of our efforts and observations should be presented.

It is not our intent to discuss either the physics of microwave propagation or its ignition hazards. This presentation will be limited to a brief discussion of the objectives, methodology, findings, and interpretation of our program.

From the Medical Department, Lockheed Aircraft Corporation.
Read before the Joint Meeting of the Section on Preventive Medicine and the Aero Medical Association at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Our objectives were threefold: (1) to detect any cumulative biological effects of long-time exposure to microwaves of varying frequency and power output in persons who had taken minimal precautions; (2) to observe possible effects on persons working for short periods of time with or near extremely high-powered airborne radar with pulsed wave emissions; and (3) to establish correlation between objective findings and units of exposure expressed in time-power density factors with the highly idealized objective of establishing safe maximum exposure standards.

Effects of Long Periods of Exposure

Our initial study included 226 radar-exposed employees and 88 nonexposed control subjects. The examination program was designed to detect in our subjects pathology similar to that observed in exposed animals and included procedures and laboratory studies previously performed by other investigators. Several additional procedures were used in an attempt to duplicate findings alleged to have been observed in a study of human subjects.

Examination in every case included an extensive system and organ inventory, with emphasis on the ocular structures, central nervous system, gastrointestinal and urinary tracts, hematopoietic system, and skin. Imbedded metallic foreign bodies were identified; a careful marital and fertility history was elicited; and duration and manner of exposure to radar was identified.

Physical examination was extensive with respect to the body systems as outlined above. In addition, each subject was inspected for manifest hemorrhagic phenomena. A modified test for Rumpel-Leede phenomenon was then performed by means of placing the blood pressure cuff on the arm and maintaining pressure midway between systolic and diastolic pressure for three minutes. The appearance of more than 10 fresh petechiae in a circle 4 cm. in diameter below the cuff was considered a positive result.

The second phase consisted of an ocular examination, including a slit-lamp study performed with the subject subjected to cycloplegia by a competent ophthalmologist; complete blood cell and platelet counts; chest x-rays; and urinalyses.

Among the radar groups were 83 with 2 to 5 years of exposure and 37 with 5 to 13 years. Many of them were exposed while in military service or with other companies prior to their employment at Lockheed. Few had observed any precautions whatsoever prior to 1953. Despite this, no pathology or adverse physiological effects unequivocally attributable to microwave exposure could be demonstrated. Minor variations in the red and white blood cell counts were comparable with those of the controls. An apparent decrease in polymorphonuclear cells and increase in eosinophils and monocytes was later found to be due to a variation of interpretation by a laboratory technician. There were no significant variations in blood platelet counts. Abnormal urinalyses were found to be proportionate in both groups.

Physical abnormalities revealed a higher percentage of circulatory and gastrointestinal diseases in the controls, with a higher incidence of jaundice, severe headaches, and bleeding phenomena. Ocular pathology was considerably greater in the radar group. However, with the single exception of a small, solitary retinal hemorrhage, which absorbed completely within three months, all abnormalities were causally related to diseases or conditions not generally associated with microwave exposure. Chest x-rays were noncontributory. Modified tests for Rumpel-Leede phenomenon were interesting in that 8% of the control group showed positive results, compared to 2% of the radar group. There was no apparent correlation between positive findings and reduced platelet counts. Findings were negative in all but one subject with platelet counts below 200,000 per cubic millimeter. The positive results were, with this single exception, in persons with normal platelet counts.

Fertility studies revealed essentially the same percentage of offspring in both groups, when correcting for the larger number of unmarried men in the radar group. The percentage of childless marriages attributable to unknown causes was comparable, and in not a single instance in the radar group could an admission of male sterility be elicited.

On the basis of these findings we concluded that no person in this study had sustained any acute or chronic injury secondary to radar exposure. Reference is made to an earlier report describing our results in greater detail.[4]

Effects of Short Periods of Exposure

The second objective of our program is currently being accomplished. Having established base-line or reference criteria, we proceeded to reexamine our personnel, first at 6-month, then at 12-month, and finally at 24-month intervals, approximately four years after the original study. This latter program is now in progress. As a result of our original study and findings it was decided to modify our procedures and eliminate several of the more costly, time-consuming, and noncontributory tests. An extensive medical questionnaire was prepared, and each subject was interviewed by a physician. Physical examinations were performed only when indicated on the basis of the medical history or laboratory studies. Ocular and slit-lamp studies were repeated, and complete blood cell counts and urinalyses were performed. Blood platelet studies were repeated on alternate years. A limited number of electrophoretic serum protein patterns were made

in an attempt to validate significant changes claimed to have been observed by another investigator.

Routine control studies were discontinued during the second and third examinations but were resumed in a limited degree during the present program. Despite a small sampling of radar-exposed personnel to date (49) it is believed that this group, under surveillance for four years and with exposure to identifiable transmitters, will provide valuable information for comparative purposes. Additional information obtained includes number of days of sick leave, leaves of absence, and other health statistics for the year 1957. Also, a large number of tests for Rumpel-Leede phenomenon were performed on applicants for employment and employees seeking treatment for routine ailments. None of these subjects had had any known exposure to radar emanations.

The results of our studies are graphically presented in the accompanying tables. Table 1 identifies radar-exposed personnel as to numbers, age group, and years under medical surveillance and compares them to the control group. The total exposure group has increased to 335 by the addition of newly hired or reclassified employees. Persons in the one-year study generally have had two examinations, in the two-year study two or three examinations, and in the four-year study three or four examinations. Only the results of the last examinations are included in subsequent tables.

Table 2 reveals the fertility history of the radar-exposed and control groups. The slightly lower percentage in the first group who have fathered children is reflected in the larger number of unmarried men in this younger age group. Of those who are married and for unknown reasons have no offspring, the control group shows a somewhat higher percentage. The average number of children per family for each group is approximately two.

Table 3 lists comparative pathology or major subjective complaints for the various groups. These conditions were present at the time of the last examination or had been present the previous year. Among the radar-exposed group, sinus, gastrointestinal, genitourinary, and dermatological complaints were most prevalent. Headaches and nervousness were the commonest subjective complaints. The control group exhibited sinus, allergic, gastrointestinal, joint, and genitourinary disease prevalence, with fewer headaches and skin and respiratory complaints. There were no marked deviations or trends from the common disorders and no unusual or unexplained hemorrhagic phenomena. Bleeding was primarily nasal, rectal, or urinary in origin, and generally of known causation.

Table 4 reveals ocular findings for the radar-exposed groups only. In our opinion not a single finding can be attributable to radar exposure. There were no cataracts characteristic of those experimentally induced in animals by hyperthermia, and the corneal scars were, in the main, associated with other known causative agents. There were no tendencies toward progressive ocular diseases, and the four-year group revealed no pathology significantly different from that of the other groups. Congenital sutural cataracts are commonly seen in the general populace and are of no significance.

Sick leave for the 49 subjects who were in the four-year group averaged 3.0 days for the year 1957, compared to 3.1 days for the entire factory. In addition, there were five absences of more than 30 days in the radar-exposed group for the following reasons: hemorrhoidectomy, herniorrhaphy, appen-

TABLE 1.—*Subjects in Medical Surveillance Program*

Age, Yr.	Exposed Personnel by Study Group, No. Single Test	1-Yr.	2-Yr.	4-Yr.	Total	Controls, No.
<20	1	0	0	0	1	0
20-29	62	15	30	5	112	12
30-39	46	24	55	24	149	52
40-49	14	8	22	16	60	30
50-58	5	1	3	4	13	6
Total	128	48	110	49	335	100

TABLE 2.—*Fertility Data for Subjects in Medical Surveillance Program*

	Exposed Personnel by Study Group							Controls		
	Single Test	1-Yr.	2-Yr.	4-Yr.	Total	Av. No. of Children	% Without Children	Total	Av. No. of Children	% Without Children
Children, no.	112	36	158	76	382	1.94	...	152	2.11	...
Fathers, no.	72	18	77	30	197	...	...	72	...	...
No children Cause known,* no.	40	14	25	17	96	...	27	...	...	10
Cause unknown, no.	16	16	8	2	42	...	13	...	...	18
Total	128	48	110	49	335					

* Major known causes: unmarried, wife sterile, birth control.

TABLE 3.—*Comparative Pathology and Number of Subjects with Major Complaints in Medical Surveillance Program*

Pathology	Exposed Personnel by Study Group (335) Single Test	1-Yr.	2-Yr.	4-Yr.	Total	Controls (100)
Nervousness	4	1	2	3	10	4
Headache	5	...	5	3	13	6
Sinusitis	6	...	5	2	13	14
Hay fever	2	...	...	2	4	10
Respiratory disease or asthma	1	...	1	...	2	8
Circulatory and coronary disease	3	...	1	1	5	4
Peptic ulcer	...	1	4	2	7	...
Other gastrointestinal disorder	2	2	7	3	14	8
Urinary tract infection	2	...	5	1	8	8
Skin disorder	4	...	1	2	7	6
Arthritis, bursitis	3	...	2	2	7	10
Bleeding (nose, rectal, urinary)	3	3	2	...	8	4
Other	2*	1†	...	1‡	4	30

* Mumps, deafness.
† Diabetes.
‡ Ruptured appendix with peritonitis (subject died).
§ Diabetes, hypothyroidism, hernia.

dectomy, nervous breakdown, and skull fracture. These longer absences represent a rate of 10% for this small group, compared to a plant-wide rate of 8%. One death occurred among the radar-exposed group; it was attributable to complications after a ruptured appendix. The diagnosis was confirmed

TABLE 4.—*Number of Ocular Findings in Radar-Exposed Groups*

Pathology	Single Test (128)	1-Yr. (48)	2-Yr. (110)	4-Yr. (49)	Total (335)
Pterygium	1	1	2	1	5
Esotropia or exotropia	5	2	3	3	13
Cornea					
Old scars	4	1	4	1	10
Keratitis bullosa	1	...	...	...	1
Lens					
Cataract, sutural (congenital)	6	2	9	2	19
Cataract, traumatic	1	1	1	...	3
Vitreous "floaters"	1	1	1	1	4
Drüsen	4	...	3	...	7
Other*	6	4	3	4	17

* Papilloma, acute trauma, telangiectasis, blepharitis; leukoma (2), episcleritis, pigment change in iris, allergic conjunctivitis; eclipse burn of macula, small retinal hemorrhage, medullated nerve fibers (3), macular scar (cause unknown); diabetic retinopathy, healed chorioretinitis, surgical ophthalmostomosis.

on autopsy, and the pathological findings were typical of the disease process. Coincidentally, there were over 200 appendectomies, for acute appendicitis, performed on company personnel during the past year. In 1957 there were 113 deaths of company employees, including several cases of leukemia and plasma cell (multiple) myeloma. There was no known exposure to microwaves in any of these cases.

Table 5 reveals blood findings in the radar-exposed groups and in the 100 control subjects. Only the last blood cell counts for the radar group are shown. It is apparent that the blood picture of the radar-exposed and control groups is comparable in most respects. An unusually high incidence of increased monocytes and eosinophils is noted. However, it is somewhat higher in the control group, and the relative increase in these cells can be traced to the interpretation of one laboratory technician.

Blood platelet determinations revealed counts of less than 200,000 per cubic millimeter in only 2 of 243 subjects tested, despite a higher incidence of reduced counts in our original study. Of the 49 subjects studied over four years, only one had a reduced count. This was unusually revealing, in view of the attempts of at least one investigator to use this as an index of exposure. Also, since the same investigator associated exposure with positive findings on tests for Rumpel-Leede phenomenon, we decided to perform these tests on persons who routinely came to the attention of our medical department. Accordingly, 145 tests were performed on employees seeking minor first-aid care, management personnel undergoing annual health examinations, and a small number of applicants for employment. No subject was included in this study if he had knowingly been exposed to microwaves during military service or employment. Of the 20 positive findings obtained, 14 were in men and 6 in women; these represented 14% of the group. Of these subjects, two presented histories of hemorrhagic tendencies, two had been exposed to considerable ionizing radiation (x-ray), three had undergone recent major abdominal or pelvic surgery, and one was taking sedative medication. Of the 88 subjects used in our original control group (in 1954), positive results were noted in 8%.

In 26 cases selected at random, electrophoresis of serum proteins was performed at a hospital laboratory. Many of these specimens were from subjects in the two-year and four-year groups. Results in 16 tests were reported within normal range for all component proteins; 10 revealed deviations as follows: elevation of gamma globulin level, 4; depression of beta globulin level, 3; elevation of beta globulin level, 1; depression of gamma globulin level, 1; and depression of alpha globulin level, 1. In only one subject was the deviation more than slight or considered significant, and this was partially reversed within two months after elimination of an active known infection. Deviations described are generally associated with dietary deficiencies, infections, or obesity. One subject had been exposed to ionizing radiation, two had known active infections, and two had undergone recent surgery.

In no case was there any significant decrease in serum albumin or total protein levels. The albumin-globulin ratio was within normal limits in all persons.

Maximum Exposure Standards

Our third objective was to delineate safe maximum exposure standards. Obviously, this was contingent on the detection of pathological changes

TABLE 5.—*Comparative Blood Cellular Findings in Subjects in Medical Surveillance Program*

	Exposed Personnel by Study Group, No.						Controls	
	Single Test	1-Yr.	2-Yr.	4-Yr.	Total	% of 335	Total	% of 100
Red blood cell count, per cu. mm.								
<4,200,000	...	9	1	1	11	3.3	0	0
4,200,000-5,400,000	20	9	11	2	42	12.5	10	10
White blood cell count, per cu. mm.								
Total								
<5,000	...	...	...	...	0	0	0	0
>10,000	18	7	21	11	57	17.0	16	16
Differential count								
Polymorphonuclear cells								
<50%	21	4	15	16	59	17.6	19	19
>70%	18	3	14	3	38	11.3	12	12
Monocytes (>6%)	13	10	10	18	51	15.4	21	21
Eosinophils (>4%)	16	4	12	16	48	14.3	16	16

in our subjects and determination of the exposure parameters with respect to frequency or wave length, field power density, exposure time, and total test environment.

It soon became apparent that this objective could not be achieved in our study. We uncovered no pathology caused by either single or repeated ex-

posure, and consequently we cannot speak authoritatively of so-called hazardous exposure conditions. The majority of our personnel had been exposed to radars of the following types: AN/APS-20A, B, C, and E; AN/APS-28, 30, 31, 33, and 45; AN/APG-40, SG, SX, and SR; AN/APS-6 and 7; and AN/APS 70. These transmitters operate in a frequency range of 400 to 9,000 mc and include powerful "S" band components. It was impossible to obtain precise data covering exposure time and average field power density, since these often were unknown. Exposure, however, varied from an occasional incidental contact with the beam to as much as four hours daily close exposure for periods up to four years. Exposures of several minutes a day at distances of less than 10 ft. from the radars were not uncommon.

Protective clothing was not worn by any of our subjects while in the radar beam. For some time precautions have been exercised in testing of our equipment and in exposure of personnel. In general, ground testing of high-powered, aircraft-mounted transmitters involves scanning of a very limited sector, with the antenna pointed toward an open, uninhabited field and rotating at 2 or 6 rpm, usually firing at reduced power.

Personnel were advised to avoid exposure to any firing beam when in a zone defined by a minimum power density of 0.0131 watts per square centimeter. A second zone, extending from the area previously defined to that with a minimum power density of 0.0039 watts per square centimeter, was deemed acceptable for occasional pass-through but no constant exposure, and, finally, there was a third limitless zone in which exposure was not deemed biologically significant.

Unfortunately, because most persons are exposed to radar emanations while on the ground and frequently within the so-called near radar field, it is extremely difficult to evaluate biological effects and hazards in relation to absolute power levels without accurate measurements. The need for such accuracy in quantitative determinations of exposure is obvious and can be achieved by the development of exposure meters reflecting absorption in quantum units of radar energy.

It has been suggested that the sensation of heat is almost universal on exposure to radar and that this in itself is indicative of an overexposure. In our study, only 17% of the 335 subjects experienced heat sensation and frequently only when in close proximity to "X" band radars. Almost 6% were aware of a buzzing or pulsating sensation when in an "S" band field. Less than 1% experienced other sensations or warning phenomena, such as sparking between dental fillings or a peculiar metallic taste. Eight subjects gave a history of metallic implants, such as bullets, buckshot, steel pins, and plates. None experienced any unusual reaction attributable to the metal. There were no complaints of heat directed to rings, wrist watches, or bracelets.

Comment

During the past 18 years thousands of persons, in the course of their employment or while in military service, have been exposed to microwaves, many without protection. Concern over the effects of such exposure is natural and to be expected. The majority of radars in common use today are relatively low powered, with the exception of some military transmitters which exceed one megawatt in peak power output. Radars with many times this power will be operational in due course and may radically change our entire concept of the biological potentials of this form of energy.

Since microwaves of varying frequency and power output are also being used to provide television display, for diathermy, and in electronic ovens, the personal safety problem is one of general public interest.

Experiments to date have been conducted primarily on small fur-bearing animals and under unusual test conditions. It is generally accepted that the modus of injury by microwaves is a hyperthermia produced by absorption of this form of energy by the body. Extreme caution must be exercised in attempting to extrapolate the results of small animal responses to heat to those of the human body. Small fur-bearing animals have a high coefficient of heat absorption, a small body surface, and a relatively poor heat regulating system. The human body, by comparison, has one of the best and can readily adjust and maintain thermal homeostasis under severe stress conditions. Adequate physiological function can be maintained in environments of 240 F for 23 minutes if the humidity is low, and at least one subject has been exposed to a temperature of 400 F, for a period of approximately one minute, without tissue injury.

Conditions of radar operation and testing vary from experimental conditions. Humans are generally exposed while in free air and rarely to a stationary energized beam. Some radar beams are extremely narrow, and only a small portion of the human body is instantaneously exposed. The body can dissipate heat readily to the environment between such exposures. One is reminded of a similar problem associated with exposure of personnel to the thermal effects of ultrasonic energy. In an analogous situation, small fur-bearing animals were destroyed by hyperthermia when placed in a jet engine noise field, yet there is no evidence of any adverse heating effects on man when exposed to the same environment. It has been estimated that it would require many million times the ultrasonic energy of that generated by any current jet engine to produce these effects in human beings.

There is reason to believe that the dramatic effects observed in small animals exposed to whole-body radiation will not be reproduced in larger, live animals under identical test conditions and that the human body will be the most resistant of all. This is not to imply that localized application of heat cannot injure human tissue. We have witnessed one case of accidental 15-second exposure, at a 6-to-10-in. distance, to an "X" band radar of over 100,000 watts in peak power output, with resultant erythema and a sensation of warmth for an hour but with full and uneventful recovery. Unless carefully controlled and operated, microwave diathermy with use of "S" band frequencies can cause local tissue damage.

In our study we have failed to detect any acute, transient, or cumulative physiological or pathological changes in subjects working with and frequently exposed to high-power radar transmitters. It would therefore appear extremely unlikely that there exists a biological hazard to the radar technician observing reasonable precautions or that the general public, exposed to greatly attenuated and intermittent doses of microwaves in the environment, is in any danger of body injury. We can see no causal relationship betwen microwave exposure and any increase in such conditions as coronary heart disease, leukemia, bone and lung cancer, and degenerative diseases of the nervous system.

There is need for additional research to explore the effects on living tissue of extended wave lengths and frequencies of microwaves and transmitters of higher energy, and military research is being directed in this area.[5] Col. G. M. Knauf has reported on the progress of this research at the American Medical Association's Annual Meeting in San Francisco. It is hoped this study will provide the basis for establishment of a realistic safety program acceptable to all scientists.

Finally, a plea is made for deductive rather than inductive research in this difficult field. With the increasing exposure to microwaves in and around the home, as well as in industry, careless and scientifically uncorroborated reports of human injury and death cannot avoid receiving dramatic and widespread dissemination. Such reports should not appear unless sufficient scientific data are included to support the conclusions and unequivocally establish the modus of injury. If radar is incriminated, the report must contain a definite history of exposure, including proper identification of the transmitter, wave length, power density, exposure time, symptomatology, laboratory data, pathological findings, and other factors.

Summary

In 1954, a medical surveillance program was instituted, covering 335 employees working with or exposed to microwaves in an airframe manufacturing company. Examinations have been performed at intervals of 6, 12, and 24 months in an effort to detect acute or cumulative biological effects of exposure at various intervals to energized radar beams in the 400-to-9,000-mc range and with peak power output exceeding one megawatt. Whenever possible, identical examinations were also accomplished on a nonexposed control group.

The examinations have failed to detect any significant changes in the physical inventories of the subjects. The incidence of death and chronic disease, sick leave, and subjective complaints was comparable in both groups. A high percentage of eye pathology was identified, but none with causal relation to the hyperthermia produced by microwave absorption. Fertility studies revealed essentially the same findings for both groups.

Laboratory studies for total red and white blood cell counts and differential counts revealed no significant changes above those noted in the control group. Urinalyses and chest x-rays were noncontributory with respect to radar exposures. Electrophoretic serum protein level determinations were performed on 26 subjects, with insignificant or accountable deviations in 10. Platelet counts and controlled capillary fragility studies for Rumpel-Leede phenomenon revealed the fallacy of using either to identify radar exposure. In addition, only a small percentage of the exposed subjects had been aware of heat or other subjective warning phenomena. Neither these tests nor subjective complaints were considered reliable indexes of exposure.

Absolute or safe maximum exposure standards were impossible to define, inasmuch as no radar-induced pathology could be identified. Subjects had been exposed for various periods, at indefinite distances, to a multitude of radars under flexible test conditions. The need for more precise and refined exposure data is indicated.

On the basis of these studies there appears to be no justification for public concern about the effects of greatly attenuated microwave energy in the environment. It would seem, therefore, that one may continue to enjoy his television without undue apprehension.

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SYNCOPE IN A POPULATION OF HEALTHY YOUNG ADULTS

INCIDENCE, MECHANISMS, AND SIGNIFICANCE

Capt. George Dermksian (MC), U. S. A. F.
and
Lawrence E. Lamb, M.D., Randolph Air Force Base, Texas

Syncope, or fainting, is a common, everyday occurrence. Both the lay public and the medical profession tend to regard it casually, due to the lack of complications and sequelae. However, in the situational environments of industry and aviation, transitory loss of consciousness may result in serious accidents and death.

In any operation involving a man-machine effort, the success of the operation depends on the man just as much as on the machine. Modern aviation is a good example wherein split-second failure on the part of the man can have disastrous results. In recognition of the importance of syncope as a cause of human failure in aviation, an effort is made to detect those persons who are syncope-prone as a preventive measure and all cases of syncope are carefully studied to ascertain the cause when possible. Among flying personnel, 82 persons who have experienced 113 syncopal episodes have recently been studied at the School of Aviation Medicine.

Method and Techniques

Studies on the 82 apparently healthy persons included the taking of a detailed history, a complete physical examination, blood cell count, determination of hematocrit value, erythrocyte sedimentation rate, and fasting blood sugar level, urinalysis, chest x-ray, skull x-ray, and electrocardiogram. Other tests have been utilized when indicated. In addition to this routine examination, 55 persons were given a battery of special procedures designed to stress the cardiovascular system. In this manner it was hoped to determine the factors which might have contributed to their syncopal episodes and also to study the disturbances in the cardiovascular mechanisms associated with syncope. The patient's blood pressure, pulse rate, symptoms, and signs were observed at rest and on a tilt table during (1) breath-holding at maximum inspiration; (2) hyperventilation followed by breath-holding; and (3) carotid sinus massage of 15 seconds' duration. A 15-minute orthostatic tolerance test on the tilt table and a one-minute cold pressor test (hand immersed in water of a temperature between 0 and 1 C) were performed. The response to intravenously given atropine, 0.75-1.2 mg., was also studied in five cases.

From the School of Aviation Medicine, Randolph Air Force Base, Texas.

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A better understanding of mechanisms precipitating syncopal episodes and their likelihood of recurrence can lead to prevention of accidents resulting from syncope and perhaps prevent syncopal episodes at crucial times. Eighty-two persons studied described a total of 113 syncopal episodes occurring sometime in the past. The factors, surrounding the acute clinical episode of syncope, were highly variable. More than one factor may have played a role in the precipitation of syncope in a large number of the cases. The overt act at the time of syncope was most often postural change or pain. Cardiac arrhythmias induced by the common respiratory maneuvers were often associated with syncope. Disturbances in a person's general hygiene not only decrease his stress tolerance but apparently make him more susceptible to syncope.

Results

The 82 persons studied in this series were U. S. A. F. flying personnel. They described a total of 113 syncopal episodes occurring sometime in the past. The factors surrounding the acute clinical episode of syncope were highly variable. The age at the time of syncope, a brief note about the clinical circumstances, and the findings during the clinical investigation are briefly summarized in the table. From the brief clinical notes it can be seen that more than one factor may have played a role in the precipitation of syncope in a large number of the cases. The overt act at the time of syncope was most often postural changes or pain. Eleven subjects had recently ingested at least one alcoholic drink prior to the syncopal episode, six had been on weight-reducing diets, and others had recently completed some exhaustive physical labor and/or lacked adequate rest. It is our impression that disturbances in a person's general hygiene not only decrease his stress tolerance but apparently make him more susceptible to syncope.

Only one of the cases could definitely be attributed to a clinical episode of cardiac arrhythmia. This is not surprising, since this was the only episode of clinical syncope monitored by an electrocardiogram.

Clinical Findings in Eighty-two Persons Who Had Experienced Syncope

Case No.	Age at Time of Syncope, Yr.	Clinical Incident Associated with Syncope	Findings on Investigative Procedures
1	31	Venipuncture	Atropine caused shift in pacemaker to atrial focus
2	12	Standing up	Near syncopal episode after release of breath-holding; cardiac rate decreased from 102 to 69/min.
	38	Fatigue, alcohol ingestion, bending over	
3	33	Alcohol ingestion	None
4	25	Standing in one position 3-4 hr.	None
5	23	Alcohol ingestion, warm, smoky room	Had syncope twice when placed on tilt table to obtain base-line blood pressure and electrocardiogram; sinus arrest with each episode and nodal escape beats
	23	Psychic trauma (dog bit by ear); alcohol ingestion; warm room	
	24	Standing	
6	22	Urination	Near syncope with marked drop in blood pressure during breath-holding; syncope on breath-holding after hyperventilation; cardiac rate decreased from 110 to 65/min.
7	22	"Influenza"; deep breath	None
8	28	Flying at 21,000 ft.	Cold pressor test caused asystole and near syncopal episode
9	14	Had a "cold"; sitting in warm room	Syncope 2 min. after right carotid massage; heart rate decreased to 30/min. with precipitous fall in blood pressure
	23	Upper respiratory infection; syncope after hyperventilation in altitude chamber	
	24	Standing at attention	
10	25	Had just arisen and was preparing to wash (later proved to have grand mal seizure)	None; EEG normal
11	24	While piloting aircraft, suddenly lost 13,500 ft. of altitude; circumstances unknown; presumably momentary loss of consciousness	Near syncopal episode with marked drop in blood pressure when base-line studies were being recorded on tilt table
12	37	Felt something in his throat and turned to cough; lost consciousness before coughing	None
13	23	Gastroenteritis	None
14	32	Unexplained loss of consciousness while piloting aircraft; suggestion of difficulty with face mask; apparently not hypoxia, as he regained consciousness and made unsuccessful attempt to control aircraft	Breath-holding at height of inspiration resulted in lower nodal rhythm and syncope
15	36	Urination; fatigue; lack of food; alcohol ingestion	None
16	39	After vomiting; history of fatigue	None
17	24	Pain	None
18	39	Sudden loss of 16,000 ft. of altitude while piloting aircraft; apparent transitory loss of consciousness in flight	None
19	37	Topical application of anesthetic to eye for tonometer measurement	Breath-holding after hyperventilation resulted in decrease in heart rate from 135 to 66/min. with syncope
20	26	Standing at attention in sun	Near syncope after left carotid sinus massage. Heart rate slowed from 90 to 66/min.
21	22	While flying at 31,000 ft. turned in seat, became nauseated and dizzy, and lost consciousness	Repeated syncopal episodes after breath-holding, associated with asystole
22	30	Was in warm room, went outside, and either slipped on ice and fell or experienced syncope	None
23	35	Alcohol ingestion; large meal; standing up	None
24	25	Venipuncture	None
25	26	Defecation; gastroenteritis	None
26	35	Exertion; dieting	None
	35	Mowing the lawn; dieting	
27	34	Standing after bending	Breath-holding after hyperventilation was associated with A-V dissociation; no symptoms
28	18	Unexplained syncope while seated playing cards	Syncope when breath-holding at height of inspiration, associated with decrease in blood pressure without significant cardiac arrhythmia
29	22	Flying at 8,000 ft.; patient does not know what happened	None
30	26	Seated after exertion; lack of food and sleep	None
31	25	Pain	None
32	23	Shaving; lack of sleep; sunburn	None
33	25	Hyperventilation at 24,000 ft. in altitude chamber	None
	27	Hyperventilation at 24,000 ft. in altitude chamber	
	30	Walking	
34	23	Seated in classroom listening to lecture on disagreeable subject	None
35	22	Called to attention	
	22	Convulsion after left carotid sinus massage	Convulsion after left carotid sinus massage reproduced without decrease in heart rate or diminished blood pressure
36	27	Standing	Breath-holding demonstrated A-V dissociation without symptoms
37	25	Standing in line for physical examination; fainted as he walked away from doctor after examination	Syncope after right carotid massage; cardiac rate decreased from 120 to 68/min.
38	28	Seated at table, rose from chair, and fainted; weight reducing; alcohol ingestion	None
39	18	Gastroenteritis	No special studies
	30	Back pain	
	30	Manipulation of back and production of pain (next day)	
40	37	Getting out of bed	No special studies
41	26	Alcohol ingestion	No special studies
42	36	Urination; had been hospitalized for possible myocardial infarction which he did not have; was watching TV program on myocardial infarction prior to acute episode of syncope; was nauseated	No special studies
43	23	Acrobatics and pulling 2½ to 3 G forces	No special studies
44	23	Aircraft let down while in hot cockpit; nauseated	No special studies
45	Childhood	Dental procedure	No special studies
	Childhood	Gastroenteritis	
	Childhood	Pain	
	Childhood	Sight of blood	
	38	Patient's child had nosebleed; patient fainted while assisting him	
	38	Venipuncture (next day)	
46	35	Straining at stool with painful bowel movement	No special studies
47	22	Acrobatics in back seat of aircraft	No special studies
48	40	Repeated near syncopal episodes with dental procedures	No special studies
49	37	Standing at racetrack watching racing cars; had been drinking with inadequate food intake; had previously been on reducing diet	No special studies
50	35	Walking into flight operations; fatigued from lack of sleep and food	None
51	23	Vomiting; became nauseated while listening to lecture on altitude chamber	No special studies
52	26	Fell out of bed and was apparently unconscious	No special studies
53	21	Local treatment of acute external otitis; developed pain and syncope	Nodal rhythm after stimulation of external ear; no other special studies
	21	Repeated syncopal episode with ear manipulation	
54	33	Gastroenteritis with dehydration and poor nutrition	No special studies
55	35	Standing after bending	No special studies
56	38	Hypoxia and hyperventilation in altitude chamber	No special studies

Clinical Findings in Eighty-two Persons Who Had Experienced Syncope—Continued

Case No.	Age at Time of Syncope, Yr.	Clinical Incident Associated with Syncope	Findings on Investigative Procedures
57	4	Hit on head with rock	No special studies
	15	Systemic febrile response to immunization	
	24	Teeth cleaned by dental technician	
58	26	Epigastric pain after eating; took several deep breaths and attempted to belch; syncope resulted	No special studies
59	21	Syncope with G forces; back pain	No special studies
60	23	Standing after extreme exertion	None
	23	Same as above	
61	23	Multiple injuries due to aircraft accident	Breath-holding after hyperventilation
	35	Pressure breathing in altitude chamber at 43,000 feet; nodal rhythm with seizure	caused syncope with decreased blood pressure; during investigation patient developed nodal rhythm with syncope; carotid sinus massage produced bradycardia with near syncope
62	24	Seated; acute gastroenteritis	No special studies
63	36	Pain	No special studies
64	Childhood	Syncope on sight of blood	No special studies
	26	Standing after bending over	
	26	Rapid decompression in altitude chamber; holding breath	
65	20	Standing during fraternity initiation after lack of sleep for 72 hr.	None
	26	Syncope resulting from G force intolerance	
66	27	Syncope on arising rapidly from bed	None
	33	Same as above	
	36	Same as above	
67	38	Pain	No special studies
	38	Manipulation of wound	
68	11	Getting out of bed after febrile illness	No special studies
	15	Standing 3 hr. in crowded room	
69	37	Pain	No special studies
	37	Bending over after exertion	
70	31	Getting out of bed	No special studies
71	27	Breath-holding rather than expiring during rapid decompression in altitude chamber	None
72	31	Sitting during lecture; lack of sleep; alcohol ingestion	None
73	22	Syncope after shower; felt dizzy	None
74	30	Vomiting; had a "cold" headache and had been drinking but denied inebriation	None
75	37	Urination	Syncope after right carotid massage and left carotid massage, with A-V dissociation and nodal rhythm
76	33	Suddenly standing	None
77	37	Starting to shave; lack of sleep; headache; chest pains	None
78	23	Apathetic episode during instrument check in aircraft; described as syncope by instructor	None
79	12	Getting out of bed after pneumonia	None
	20	Near syncope during venipuncture	
80	26	Flying; looking at radarscope	None
81	30	Standing in hospital room visiting son after tonsillectomy	None
	34	Standing at bar; syncopal episode after one drink	
82	21	Had a "cold"; chest being examined by physician; deep breaths	Breath-holding produced depression of SA node and shift to atrial focus followed by A-V dissociation; one episode of marked sinus depression with only one sinus impulse occurring over 6-sec. period; cardioinhibitory response prevented by atropine

Of the 55 subjects examined by the special techniques, 16 had a syncopal or near syncopal episode during the investigative procedures. An additional subject (case 53) had the onset of a nodal rhythm during external ear stimulation which resulted in syncope. This subject was not otherwise examined by the special technique. Of the 17 subjects who developed experimental syncope, in 13 the incident was associated with a cardiac arrhythmia or a marked decrease in cardiac rate. Four persons had syncope with insignificant changes in the cardiac rhythm.

In this series of 55 subjects, 17 developed a cardiac arrhythmia or marked cardioinhibitory response with or without syncope. Breath-holding induced cardiac arrhythmia in nine cases, including three examples of marked sinus bradycardia. In six of the nine cases the arrhythmia was associated with syncope. Breath-holding caused syncope in eight individuals. In one of these it was chiefly a vasodepressor response without significant arrhythmia.

It is interesting to note that 13 of these subjects experienced clinical syncopal episodes during flight. Five instances were attributed to G forces. Of the remaining eight persons, four developed experimental syncope associated with significant cardiac arrhythmias (cases 8, 11, 14, and 21).

Since syncope is regarded so casually by both the lay public and the medical profession, it is difficult to obtain many facts concerning its incidence or much factual information concerning its causes. The clinical histories of these 82 subjects point up the varied and intangible circumstances that might surround any syncopal episode.

Incidence

Very little information is available concerning the expected incidence of syncope in the general population or in various age groups. Guzman-Perry [1] studied 300 healthy young male students at college and postgraduate levels of training. He found a 15.5% incidence of fainting. Collins [2] studied a group of basic trainees in the U.S.A.F. and reported an incidence of 0.8% in applicants and 22.3% in nonapplicants for flying training. He attributed this discrepancy in incidence in two basically similar groups to the withholding of information on the part of the flying applicants, since a history of fainting would disqualify them for flying training.

Since the true incidence of syncope in any population has not been established, 5,000 questionnaires were sent to Air Force personnel. The questionnaires were to be returned unsigned in order to avoid any motivation to withhold information. In this manner it was hoped to obtain an incidence of syncope in an apparently healthy, young adult male population. Of the 5,000 questionnaires sent out, approximately 60% were returned. The age range of this population was 17 to 62 years, with an average age of 29.1 and a mode of 27.2. The reported incidence of true syncope in this study was

7%; loss of consciousness due to a severe blow to the body or head was found in 4% and both in 0.7% of the cases. The incidence of true syncope and loss of consciousness due to severe bodily trauma is broken down for the various age groups

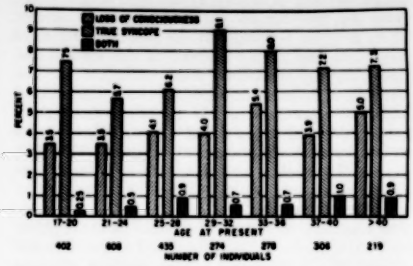

Fig. 1.—Incidence of syncope and loss of consciousness due to severe bodily trauma, by present age.

and presented in figures 1 and 2. It is recognized that a number of statistical objections could be raised against any such questionnaire survey. Nevertheless, the incidence of syncope in the returned questionnaires is interesting, even though it probably is not an exact incidence figure.

Mechanisms of Syncope

It is difficult to classify syncope because of the large number of possible underlying disorders and the variability of the acute precipitating factors. Weiss,[3] in 1935, presented a comprehensive study and discussion of syncope and syncope-like episodes. A more recent monograph by Engle [4] discusses the mechanisms and clinical characteristics of various types of loss of consciousness in the light of current physiological and psychological concepts. Many authors have chosen to consider or discuss one specific type of syncope.[5]

We have found the following classification of syncope to be simple and useful. It is based primarily on physiological mechanisms rather than on specific etiologies. Most mechanisms resulting in syncope can be grouped into one of six general categories: (1) venous (inadequate return of blood to the left heart), including systemic and pulmonary; (2) cardiac (ineffective pumping action); (3) loss of arteriolar tone (change in routing of blood flow); (4) blood qualitative changes (abnormalities in the constituents of the circulating blood); (5) blood quantitative changes (inadequate circulating volume); and (6) central nervous system (local disorders). More than one mechanism may be involved in any single episode of syncope, e. g., cardioinhibitory response with arteriolar dilatation.

Deficiencies in Venous Return.—Deficiencies in venous return, both in the systemic and pulmonary circulation, may result in syncope. Large varicosities of the lower extremities may trap blood peripherally, resulting in inadequate venous return, diminished cardiac output, and loss of consciousness. Venous pooling is one of the factors in orthostatic hypotension which contributes to syncope. Pressure breathing and the Valsalva maneuver may also inhibit adequate venous return.

The inspiratory effort at the onset of the Valsalva maneuver creates an increase in the negative intrapleural pressure and results in an initial increase in venous return to the right heart. This, in turn, causes an increased output of the right side of the heart. This increased output is trapped in the overexpanded pulmonary vascular bed, resulting momentarily in diminished venous return to the left side of the heart and diminished output on that side. Bearing down against the closed glottis tends to increase the intraalveolar pressure and squeeze the blood trapped in the lungs into the left side of the heart. The increased intrathoracic pressure inhibits further venous return to the right side of the heart, resulting in inadequate venous return. This is only one of the effects of the Valsalva maneuver. The breath-holding and resultant vagal stimulation may induce a cardioinhibitory response; this will be discussed below.

Other factors which may influence venous return to the left side of the heart include pressure breathing, visceral pooling, changes in venous tone secondary to orthostatic influences, and perhaps, to some extent, G forces. In this series of 82 patients not one example of varicosities could be implicated as contributing to or resulting in a syncopal episode. This would be expected because the subjects were initially selected as a healthy population. In addition, there were no cases which could be attributed solely to venous factors. A combination of venous and arteriolar factors are probably present in most postural or orthostatic adjustments and in tolerance to G forces. The one example of syncope after a Valsalva maneuver in this series may have been due to a deficiency of venous return and/or may have been associated with a cardiac arrhythmia.

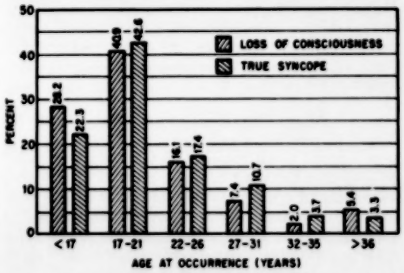

Fig. 2.—Percentage of episodes of syncope and loss of consciousness due to sever body trauma, by age of occurrence.

Ineffective Pumping Action of Heart.—Disturbances in the heart's pumping action may be due to disease of the endocardium, myocardium, or pericardium. In addition, a large variety of arrhythmias may result in syncope. In this healthy young adult male population, one would expect the incidence of syncope secondary to cardiac disease to be quite low, due to the previous screening examinations. None of the clinical syncopal episodes in this series could be attributed to underlying heart disease. Some, however, may have been due to cardiac arrhythmia, but this point can not be proved or disproved without better knowledge of the cardiac rhythm at the time of clinical syncope. In contrast, in evaluating the cardiovascular status of the subjects in this report, it was impressive to note the high incidence of cardiac arrhythmias associated with experimental syncope. By far the majority of these were induced by respiratory maneuvers, i. e., breath-holding or hyperventilation followed by

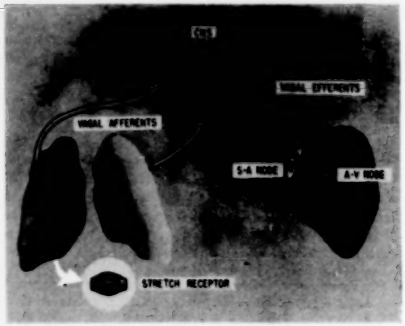

Fig. 3.—Diagrammatic representation of pulmonary-cardiac stretch reflex.

breath-holding. These cardiac arrhythmias were induced in persons whose cardiac status was otherwise normal in all respects. It was also impressive to note that the most common method of inducing experimental syncope in the battery of special tests used was the breathing maneuvers. The majority of the arrhythmias were of the cardioinhibitory type. Two examples of cardiac arrest were noted (up to 12 seconds' duration) after simple breathing maneuvers. It has previously been demonstrated that significant cardiac arrhythmias may be induced by respiratory maneuvers, even with the subject in the recumbent position.[6] This fact argues against the response being solely a postural one.

It is thought that the respiratory stimulation of the vagus nerve is the principal means of inducing the cardioinhibitory response in these individuals. The receptors and nerve pathways of such a reflex have been described. It is known as the pulmonary stretch reflex. Stretch receptors are located in the tracheobronchial tree, peripheral pulmonary parenchyma, and the visceral and parietal pleura. The receptors are stimulated by various respiratory maneuvers but primarily by inflation of the lungs. Impulses are carried via vagal visceral afferent fibers to their terminals in the sensory nucleus of the vagus and in the nucleus of the tractus solitarius. At this point their fibers come into relation with the neurons from the respiratory, vasopressor, and vasodepressor centers. Pathways from these centers descend to the spinal cord and also connect to the dorsal motor nucleus of the vagus. The efferent arc of this reflex is mediated via vagal autonomic fibers which arise from the dorsal nucleus as preganglionic fibers and go to the cardiac plexus. Postganglionic inhibitory fibers arise from the plexus and terminate in the sinoatrial and atrioventricular nodes.[7] The right vagus has its primary effect on the sinoatrial node and depresses impulse formation there, while the left vagus decreases the relative refractory period of the atrioventricular node (fig. 3). In most individuals stimulation of the stretch reflex results in varying degrees of cardiac slowing. Maximum slowing of the heart rate usually occurs at the height of the inspiratory effort. The efferent pathway for the pulmonary stretch reflex is the same as the efferent pathway of the carotid sinus reflex. The reflex can similarly be expected to cause a cardioinhibitory and/or a vasodepressor response.

It has been demonstrated that the cardioinhibitory response in susceptible individuals can be abolished by the administration of therapeutic doses of atropine (0.75-1.2 mg.). After adequate administration of atropine, other forms of cardiac arrhythmia induced by respiratory maneuvers could be prevented. In one example impending syncope was terminated by the intravenous administration of 1.2 mg. of atropine.

Atropine has been used by many investigators to induce syncope in subjects on the tilt table by increasing arteriolar and venous pooling.[8] When experimental studies are done in this manner, it is not likely that cardiac arrhythmias will be noted, as atropine will prevent the expected cardioinhibitory response. In this study a high incidence of cardiac arrhythmias was noted because atropine was not administered until after the breathing maneuvers and other stresses were carried out.

The demonstration that cardiac arrhythmias and syncope may be induced by stimulation of the pulmonary stretch reflex has direct application to any occupation, activity, or medical procedure which may involve simple respiratory maneuvers. It is common practice in aviation to use pressure breathing. The susceptible person may have a hyperactive response to stimulation of the pulmonary

stretch reflex inducing cardiac asystole and syncope. Hyperventilation is not uncommon on exposure to altitude. The pilot who holds his breath when hyperventilation is noted may stimulate the pulmonary stretch reflex, induce a cardiac arrhythmia, precipitate a syncopal episode, and be listed as having an unexplained aircraft accident. At least three unexplained sudden deaths are known to us which have occurred in persons engaged in breath-holding in underwater swimming or diving.

Artificial respiration in the operating room is an everyday occurrence. The lungs are regularly inflated by the anesthesiologist. Cardiac arrhythmias and, in fact, cardiac arrest are not unknown in the operating room. It is suggested that one of the mechanisms which may induce cardiac arrest at the time of surgery is stimulation of the pulmonary stretch reflex during artificial respiration. Small preoperative doses of atropine (0.4 mg.) are inadequate to abolish the vagal effect of the pulmonary stretch reflex.

It is possible that intermittent postive-pressure breathing, as used on medical wards, may also stimulate this reflex in susceptible individuals and could result in cardiac arrhythmia and syncope.

As is often the case, man discovers empirically methods of protecting himself when exposed to new or strange environments. Early in aviation, it was learned that the Valsalva maneuver could produce syncope. A modification of the Valsalva maneuver, now termed the M1 maneuver, was found to be most useful in increasing G tolerance during flight. In this M1 maneuver, after a deep breath is taken, rather than holding the breath in deep inspiration the person expires forcefully against a partially closed glottis, resulting in a loud yell or scream. Not only may exhaling in this manner immediately after inspiration favorably influence the mechanical factors associated with circulation, but also it abolishes further stimulation of the pulmonary stretch reflex. Thus, a correctly performed M1 maneuver serves to protect against development of significant cardiac arrhythmias which may be induced by the simple Valsalva maneuver.

Loss of Peripheral Arteriolar Resistance.—The third basic mechanism which may result in syncope is a loss of peripheral arteriolar resistance. Pain, alcohol, and true orthostatic hypotension are some examples which may affect arteriolar tone. In addition, everyone is familiar with the sensation of lightheadedness first experienced on arising after having been confined to bed for an acute illness. Any febrile illness may also decrease normal arteriolar tone, as may heat, exhaustion, or fear. Mechanical influences, such as positive G forces, may overcome normal peripheral resistance. Disturbance in arteriolar tone appears to be one of the more frequent mechanisms involved in clinical syncope. Peripheral arteriolar resistance may also be diminished in association with cardioinhibitory responses. In experimental syncope induced in these studies, a number of subjects were noted to have both a marked fall in blood pressure associated with decreased arteriolar tone and cardioinhibitory response with decreased heart rate.

Qualitative Changes in Circulating Blood.—A fourth group of contributing or sole etiological factors in clinical syncope includes qualitative changes in the circulating blood. This includes such factors as toxins, hypoxia, changes in acid-base and electrolyte balance, and anemia. In this series, direct toxins, carbon monoxide, and hypoxia were found to be infrequent causes of syncope despite the fact that all the subjects were flying personnel. True hypoglycemia could not be demonstrated to be the cause of a single episode of syncope. This may be due to the fact that hypoglycemia is more frequently associated with disturbances in mental state rather than true syncope.[9] It is possible that those individuals with relatively low blood sugar levels have a diminished tolerance to stress and are therefore more syncope-prone. When a significant anemia is present, cardiac output is increased and circulation time is decreased. This is a compensatory mechanism to provide adequate oxygenation to the body tissues, including the central nervous system. Under normal circumstances the circulatory system could perhaps adjust to a given stress. When an underlying anemia is present, the circulatory system is already compromised and the same amount of stress is capable of producing syncope.

Quantitative Change in Circulating Blood.—Decreases in the amount of the circulating blood may cause an individual to be more syncope-prone. Acute blood loss is the most obvious cause of decreased circulating blood volume. Dehydration from any cause may also diminish the circulating blood volume. In 7% of the clinical episodes of syncope in this series, dehydration secondary to gastroenteritis was a sole or major contributing factor.

Disorders of Central Nervous System.—Disorders in function of the central nervous system comprise another large group of causes of clinical syncope. This includes hemorrhage, e. g., from berry aneurysm in young persons, cerebral thrombosis, tumor, infection, metabolic changes, convulsive disorders, and other diseases of the brain and spinal cord. During experimental procedures carried out on two of the subjects in this series, it was clearly demonstrated that cardiac arrhythmias producing changes in circulatory dynamics preceded any evidence of central nervous system malfunction. In both cases an electroencephalogram was recorded and showed changes only after significant circulatory abnormalities had occurred.

Since the pulmonary stretch reflex's role in the production of cardiac arrhythmia and syncope is relatively unknown and was the most frequent cause of experimental syncope in this series, two cases illustrating this mechanism are presented.

Report of Cases

Case 21.—A 23-year-old pilot lost consciousness while flying between 31,000 and 37,000 ft. (cabin altitude 10,000-12,000 ft.) in a B-47. The aircraft had been airborne approximately seven hours, and he had been breathing oxygen. While seated, he turned to the right to "shoot the stars" when he noted the onset of nausea and dizziness. The next thing he remembered was someone reaching over him to check his oxygen equipment. He had lost consciousness and slipped to the floor. There were no other associated signs, symptoms, or residuals. The flight was terminated, and one-half hour later the patient was examined by a physician. Physical examination and laboratory studies were unremarkable.

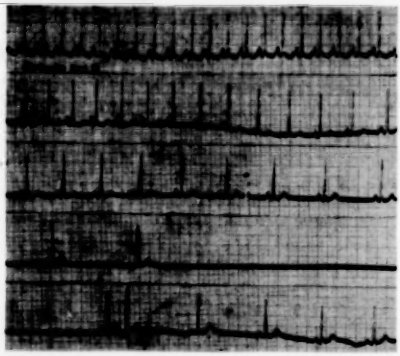

Fig. 4 (case 21).—Continuous recording of standard lead 2 during breath-holding. Nine-second period of asystole was associated with syncope. Episode was terminated by tilting of patient to horizontal position.

Subsequent follow-up and extensive diagnostic studies, including hematology, urinalysis, chest and skull x-rays, determination of blood sugar level, electrocardiogram, and electroencephalogram, were unremarkable. During the special syncope studies, when the patient took a deep breath and held it his cardiac rate slowed from 116 to 100 per minute. With the onset of breath-holding, there were two ventricular premature contractions in bigeminal fashion. The conduction then changed from sinus tachycardia to atrioventricular dissociation. After 27 seconds of breath-holding, the rate suddenly decreased to 60 per minute, and at the 36th second a six-second period of asystole followed by a sinus escape beat occurred. The patient was pale, perspiring, and clammy. After 47 seconds of breath-holding he released his breath and the shift was made to sinus bradycardia with a rate of 48 per minute. His mentation was slow, and he complained of "dizziness." At the 16th second of the recovery period he developed a three-second period of asystole, terminated with one sinus beat and followed by another three-second period of asystole. This was followed by three sinus beats and a 12-second period of asystole. The period of cardiac arrest was terminated by two ventricular impulses. During the period of asystole the patient lost consciousness. He was tilted to the horizontal position, and a normal sinus rhythm reappeared. The patient recovered.

After suitable periods of recovery, essentially the same series of events were reproduced with hyperventilation immediately followed by breath-holding and by breath-holding alone. The only difference was the appearance of nodal escape beats during the periods of asystole. With 0.75 mg. of atropine, the above sequence of events was prevented on two occasions.

Five days after the initial studies, the patient returned for repeated study. Again, whenever the patient held his breath his cardiac rate slowed, changed to atrioventricular dissociation, and then periods of asystole developed which were associated with a disturbance of or actual loss of consciousness (fig. 4). Atropine again prevented the development of arrhythmia and the loss of consciousness on two occasions.

Case 82.—A 21-year-old aviation cadet visited his flight surgeon because of symptoms and signs of an upper respiratory infection. His oral temperature was 101 F (38.3 C). During auscultation of his chest, the patient was asked to breath deeply and then to hold his breath. He apparently began to sway and had to be helped to a chair. The cadet then became flaccid and lost consciousness. Examination of the heart revealed a rate of 48 per minute and an irregular rhythm. Within 10 minutes an electrocardiogram was taken and blood drawn for determination of blood sugar level. These and other studies showed findings within normal limits.

He was hospitalized for four days and treated for his upper respiratory infection. No other abnormalities were noted on extensive physical and laboratory examination. There was no previous history of syncope or seizures.

The patient was referred to the School of Aviation Medicine where physical examination and laboratory studies, including hematology, urinalysis, determination of fasting blood sugar level, routine electrocardiogram, Master's double exercise tolerance test, altitude chamber flight with electrocardiogram, and skull and chest x-rays, were unremarkable. During the special cardiovascular studies, on every occasion that the patient held his breath during inspiration, on or off the tilt table and with and without preceding hyperventilation, his cardiac rate would suddenly slow. There would be a shift in the pacemaker either to another area in the sinoatrial node or to an atrial focus. With continued breath-holding, the pacemaker would revert to the original focus. This shift in pacemaker would occur two or three times during one period of breath-holding.

During one of these periods of breath-holding, while the patient was standing, there was a sudden slowing of the cardiac rate from 118 to 60 per minute. Associated with this, the patient became pale and began to perspire. In the next three seconds, the cardiac rate further slowed, to 40 per minute, and then there was a three-second period of asystole terminated by one normal sinus beat and followed by another three-second period of asystole. The cadet began to sway, his mentation was slow, he was cold and clammy, and syncope appeared imminent. He was placed in bed and recovered rapidly. The cardiac rate returned to 90 per minute. One atrial premature contraction appeared, followed by atrioventricular dissociation, and the pacemaker then shifted to a secondary focus. Over the next 30 seconds of recovery, atrioventricular dissociation reappeared. The pacemaker again shifted to the secondary focus and finally returned to the primary focus in the sinoatrial node. These changes in rate and conduction appeared with the patient in bed (fig. 5).

Atropine (0.75 mg.) was administered intravenously on two occasions in an attempt to prevent the changes in conduction and rhythm associated with breath-holding. On both these occasions changes in conduction, rhythm, and syncope did not occur.

Summary and Conclusions

Although syncope may be considered lightly under many circumstances, its occurrence in industry, in an automobile, and in aviation may cause a major disaster. A better understanding of mechanisms precipitating syncopal episodes and their likelihood of recurrence can lead to prevention of accidents resulting from syncope and perhaps prevent syncopal episodes at crucial times.

This report is an analysis of syncope occurring in flying personnel. Extensive studies were done in 82 subjects to ascertain the mechanisms involved in their syncopal episodes.

It has been found convenient to consider mechanisms precipitating syncope under six general types of disorders: (1) inadequate venous return; (2) inefficient cardiac pumping action; (3) loss of arteriolar tone; (4) abnormalities in the constituents of the circulating blood (qualitative blood changes); (5) inadequate circulating blood volume (quantitative blood changes); and (6) local disorders of the central nervous system. More than one of these mechanisms may be involved in any episode of syncope.

The cardiac arrhythmias are a major factor in causing inefficient pumping action of the heart. This report emphasizes the frequency of cardiac arrhythmias induced by the pulmonary stretch reflex. The stretch reflex is stimulated by common breathing maneuvers such as breath-holding and also by pressure breathing. Susceptible persons may have various cardiac arrhythmias and/or loss of peripheral arteriolar resistance with subsequent loss of consciousness. This simple chain of events may be responsible for some unexplained deaths occurring in activities involving breath-holding, e. g., underwater swimming. The stretch reflex may be stimulated after prolonged exertion. It is of particular importance in all occupations involving pressure breathing, altitude exposure, and other forms of respiratory stimulation. It is suggested that the stretch reflex may play a significant role in the operating room by producing cardiac arrhythmias and cardiac arrest during artificial respiration.

The vagal response to the stretch reflex is abolished by atropine administration. Recognition of the role of the stretch reflex in syncope and cardiac arrest, as well as a means of its prevention, has immediate application in industry and medicine.

422 W. 115th St., New York 25 (Dr. Dermksian).

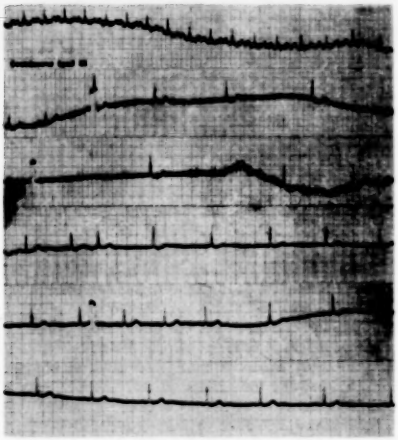

Fig. 5 (case 82).—Standard lead 2 recorded during breath-holding in standing position (first three graphs), and during recovery period (second three graphs) while patient was lying in bed. Periods of asystole were associated with near syncopal episode.

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SIDE-EFFECTS NOTED IN TREATMENT WITH METHYLPREDNISOLONE (MEDROL)

REPORT OF SEVENTY-SEVEN CONSECUTIVE CASES

F. Gilbert McMahon, M.D.
and
Edgar S. Gordon, M.D., Madison, Wis.

Sixty-seven patients and 10 healthy volunteers received treatment with methylprednisolone, with special attention to its side-effects. The largest groups of patients in the series were those with rheumatoid arthritis (18), intrinsic asthma (14), and disseminated lupus erythematosus (10). The purpose was to see whether the drug could be given in doses sufficient to exert the anti-inflammatory and other therapeutic effects of prednisone and prednisolone without widespread functional disturbances. Disturbances of body weight occurred in 40 subjects, with obesity in 14. Acne was seen in 9 and mental changes in 8; a variety of other symptoms are here tabulated. Ten cases are reported in detail, showing both the desired and the undesired effects of the drug. It promptly reduced the photophobia, lacrimation, and discomfort of the three patients with exophthalmos, but it also produced rounding of the face with other symptoms of adrenal cortical hyperfunction. Attempts to avoid these unpleasant effects by reducing the dosage led each time to the immediate return of the original symptoms. There is evidence that methylprednisolone has a stronger anti-inflammatory effect than do prednisone and prednisolone, but each patient must be evaluated carefully before it is used, and the minimal effective doses should be used for the smallest necessary time interval.

The corticosteroids are firmly established in the medical armamentarium as useful drugs in a variety of diseases. Other than as replacement therapy for adrenal insufficiency, their main application arises from their anti-inflammatory effect. Their usefulness is limited by their toxicity, and the potential hazards of steroid administration must be recognized by the physician who elects to use them. Since the introduction of cortisone in 1949 and hydrocortisone in 1951, chemical tailoring of these two molecules has been aimed in two directions: to increase the anti-inflammatory action and to decrease the side-effects (defined here as simply exaggerated manifestations of the usual physiological effects of these compounds). In the latter area, particular attention has been given to sodium retention and potassium diuresis. The synthesis in 1955 of the delta-1 steroids, prednisone and prednisolone, increased the anti-inflammatory action approximately threefold while reducing the chief undesirable side-effects. In 1957 a methyl radical was attached to the number 6 carbon atom of prednisolone to produce methylprednisolone (Medrol). Animal studies [1] showed this drug to possess from two and one-half to five times the anti-inflammatory action of prednisone. Feinberg and co-workers [2] reported that the maintenance dose of methylprednisolone in treatment of allergic diseases was about the same as or slightly lower than that of prednisone. DiRaimondo and Forsham [3] have reported this drug to have 33% greater anti-inflammatory effect than prednisolone and 60% more than prednisone.

Since there has been no previous publication devoted to the clinical side-effects of this potent new corticosteroid, we are reporting our experience in treating 77 consecutive patients with this drug. Selected case reports are also given.

Clinical Material

Sixty-seven patients at the University of Wisconsin Hospitals and Student Infirmary and 10 normal subjects, who were part of a metabolic study conducted at the Lackland Air Force Base Hospital, constitute the series reported in these observations. In the 67 patients, the conditions being treated were as follows: rheumatoid arthritis, 18; disseminated lupus erythematosus, 10; intrinsic asthma, 14; chronic ulcerative colitis, 6; hemorrhagic diseases, 3; exophthalmos, 3; chronic relapsing uveitis, 1; serum sickness, 2; sarcoid of Boeck, 1; farmer's lung, 1; malabsorption syndrome, 1; angioneurotic edema, 1; atopic eczema, 1; herpes zoster, 1; poison ivy, 4.

Dosage of methylprednisolone and duration of treatment are given in the table. All patients were on general diets unless otherwise indicated, although an attempt was made to increase calorie and protein intake in the underweight and diminish

From the departments of student health and medicine, University of Wisconsin Medical School.

calorie consumption in the obese persons. Most of the patients were initially hospitalized and subsequently followed up at regular intervals as outpatients. Others were seen at intervals of one week to one month as outpatients. A special effort was made to note the side-effects. Serum electrolyte balance and urinary glucose level were measured at least once monthly. Upper gastrointestinal x-rays with use of barium-contrast medium were not obtained unless epigastric symptoms appeared, and then stools were also examined for occult blood and red blood cell indexes obtained.

Results

All the side-effects observed are listed in the table. It is not the purpose of this paper to cite the therapeutic results obtained with methylprednisolone, but, in general, these compared favorably with those of prednisone and prednisolone. Not infrequently, however, somewhat smaller doses of the methyl derivative were successfully substituted for the delta steroids with comparable anti-inflammatory effect, indicating a higher potency of methylprednisolone. Our experience in using methylprednisolone in disseminated lupus erythematosus and rheumatoid arthritis will be the subject of another paper. Some of the important side-effects will be described here in detail.

Obesity.—Fat distribution characteristic of that seen in patients with adrenal cortical hyperfunction with Cushing's syndrome was noted in 14 patients. 4 of whom had had this finding prior to methylprednisolone administration. In two of these patients there was believed to be some diminution of the supraclavicular and cervical fat pads and moon face. Although individual variation was noted, it appeared that doses exceeding 12 mg. per day for periods of two months or longer could be expected to produce this type of obesity in most patients.

Hypertension.—Hypertension was not a significant finding in this study. Nine patients had preexisting hypertension, and no exacerbation was noted with therapy. Several patients with lupus erythematosus had progressive hypertension which was thought to be due to their underlying disease and not to the drug, since increasing the dose did not aggravate the hypertension nor did decreasing the dose diminish it. In only one patient was there a rise in blood pressure which was considered to correlate with the dose of the drug. This was in an elderly man with chronic ulcerative colitis in whom a previous labile hypertension had been noted and in whom hypertension had also followed ACTH therapy prior to the use of methylprednisolone.

Electrolyte Balance Changes.—No serum sodium or potassium level changes that could be attributed to methylprednisolone were observed. Ten young Air Force volunteers received methylprednisolone for one week as part of a more detailed metabolic study (to be reported later). Each of the patients was male, between the ages of 18 and 23 (with two exceptions, ages 39 and 41), and had normal renal, cardiovascular, hepatic, and endocrine functions. Under carefully controlled conditions, these metabolic studies during methylprednisolone administration at both 16 and 32 mg. for 24-hour levels showed that sodium clearance was slightly decreased, potassium clearance was not significantly altered, creatinine clearance was slightly increased,

Side-effects Noted from Methylprednisolone in Seventy-seven Patients

	Patients, No.	Dose, Mg./Day	Duration of Therapy, Mo.	Comment
Obesity (moon-face, fat pads)	14	12-28	3-7	Preexisted in 4 from previous steroid therapy
Hypertension	1	8	3½	Previous labile hypertension
Striae	1	24	4	
Purpura	0			
Plethora	7	12-28	2-7	
Hypertrichosis	7	6-32	2-7	
Acne	9	8-28	2-7	
Osteoporosis	0			All patients studied 1-7 mo. were ambulatory
Edema	0			
Serum electrolyte balance changes	0			
Weight gain	30			
	10	16-32	1 wk.	Normal subjects in metabolic study; av. gain, 1½ lb. (0.7 kg.)
	6	8-16	1-7	Ulcerative colitis group; av. gain, 10 lb. (4.5 kg.)
	14	4-16	1-6	Collagen disease; some on high-protein, high-calorie diet; av. gain, 5-18 lb. (2.3-8.2 kg.) without edema
Weight loss	10	4-28	1-7	6 with arthritis also on weight-reduction diets; in 2 with lupus erythematosus attributed loss to severity of underlying disease
Convulsions	2	16	4-7 days	1 also had uremia & lupus erythematosus; other was known epileptic (case 1)
Glycosuria	1	14	4	Transient, normal glucose tolerance findings
Infections	0			
Thrombophlebitis	1	16	1	51-year-old man with ulcerative colitis
Headache	0			Several with hypertension had headaches not attributable to drug
Menstrual changes	0			
Mild GI symptoms (bloating, dyspepsia)	4	6-32	1-4	Upper GI x-rays negative; symptoms relieved with antacids
Peptic ulceration	2			
	1	16	4 days	Complicated by previous prednisone therapy associated with epigastric symptoms, hematuria, and by subsequent intravenously given hydrocortisone; autopsy diagnosis (case 3)
	1	28	4	
Chronic hypercortisonism*	1	12-28	7	Case 1
Mental changes	8			
Mild personality change	5	12-32	2-7	Euphoria, mood-swings, increased doctor-dependence
Depression, insomnia, restlessness	3	12-28	4-6	Mitigated by decreasing dose when necessary
Acute psychosis	0			

* Generalized myalgia, arthralgia, crying spells, emotional mood-swings.

and aldosterone excretion was not significantly altered. It was concluded from this study that methylprednisolone has very little effect on sodium or potassium clearance and excretion in these doses and during the brief time interval employed.

Weight Changes.—In the metabolic study with 10 normal patients, there was an average weight gain in one week of 1½ lb. (0.7 kg.). Of the 10 patients with disseminated lupus erythematosus, 7 gained weight (3 to 16 lb. [1.3 to 7.3 kg.]) and two lost weight (4 to 10 lb. [1.8 to 4.5 kg.]) during treatment. Seven patients with rheumatoid arthritis gained 5 to 18 lb. (2.3 to 8.2 kg.), without discernible edema, while on high-protein, high-calorie diets. Eight patients with this disease lost weight; six were on reduction diets, and the remaining two lost 5 and 7 lb. (2.3 and 3.2 kg.) respectively.

Glycosuria.—Only one patient developed glycosuria noted on a routine outpatient visit. A subsequent glucose tolerance test while the patient was still receiving 14 mg. per day of methylprednisolone was within the normal range.

Infection.—At least two chest x-rays were available for each patient treated for a period of longer than two months. There was neither evidence of exacerbation of latent infection nor masking of known infection.

Steroid Ulcers.—Because it was deemed desirable to note any ulcerogenic effect, no patient was given a bland diet, antacids, or anticholinergic drugs when methylprednisolone was administered. Four patients complained of bloating and dyspepsia. Results of upper gastrointestinal x-rays with barium were negative. One was receiving 32 mg. per day, another 16, and two were receiving 12 mg. per day of methylprednisolone when their symptoms appeared. When roentgenographic findings were negative, they were given antacids four times daily, with the disappearance of their symptoms, while steroid therapy was continued. One patient experienced reactivation of an old duodenal ulcer with mild hemorrhage while on therapy with 28 mg. per day of methylprednisolone (see case 3 below). Two of the Air Force subjects in the metabolic study had previously proved duodenal ulcers. Neither developed epigastric symptoms or tenderness while receiving either 16 or 32 mg. daily during the weeks of study.

Psychotic Episodes.—No episodes of acute psychosis were precipitated during this study. However, mild personality changes developed in five patients, characterized by mood swings, some euphoria, and increased doctor-dependence. Three of the patients noted insomnia. One individual who had disseminated lupus erythematosus complained bitterly of restlessness and emotional upset, with periods of weeping and depression, while at other times having a sense of euphoria. It was concluded that she was manifesting chronic hypercortisonism, and her symptoms were improved with a slow reduction of dosage (see case 1 next column).

Report of Cases

Case 1.—A 39-year-old woman with a diagnosis of disseminated lupus erythematosus has been followed for four years. She has persistently had positive findings on L.E. cell preparations, hyperglobulinemia, polyarthritis, hypertension, maculopapular facial rash, and abnormal urinary sediment. She had also had pleural effusion, pericarditis, and congestive heart failure. She was treated satisfactorily with salicylates and/or chloroquine phosphate for the first year and one-half, but cortisone was deemed necessary in August, 1955, and since that time she has received one or another of the corticosteroids. In November, 1957, she developed symptoms that were compatible with a diagnosis of chronic hypercortisonism (myalgia, arthralgia, emotional disturbances, and a peripheral neuropathy manifested by shooting pains in the legs, hyporeflexia, hypalgesia, and hypesthesia with a stocking-like distribution). These symptoms were superimposed on previous features similar to those of patients with adrenal cortical hyperfunction with Cushing's syndrome, so that the possibility of their being caused by steroids was seriously entertained. Efforts to achieve good results with a reduction of the dose of prednisone to below 20 mg. per day failed. However, 16 mg. per day of methylprednisolone was successfully substituted. Over the next four weeks she was able to reduce this to 12 mg. per day, but no further reduction was possible. Indeed, in 10 weeks her condition again escaped control, and it was necessary to increase the dose to as high as 28 mg. per day. During the first month of receiving doses of 20 mg. per day or more, she complained of hypertrichosis, insomnia, and severe restlessness. These symptoms diminished during the subsequent two months, and she was maintained satisfactorily on therapy with 14 mg. per day. Although this patient had shown progressive hypertension during the course of her disease and required vigorous antihypertensive therapy, no change in the degree of hypertension was observed with either increase or decrease in the dose of methylprednisolone, so that the hypertension would appear to be a part of her underlying disease and not drug-induced or drug-aggravated.

Case 2.—A 22-year-old university student had received 1,200,000 units of benzathine penicillin because of a positive finding of beta hemolytic streptococcus on throat culture. Fourteen days later he developed severe polyarthritis, generalized pruritic, morbilliform rash, generalized lymphadenopathy, and severe edema of the face, hands, and feet. This was not relieved by penicillinase injections, antihistamines, or ephedrine. He was given 4 mg. of methylprednisolone every six hours and was completely free of symptoms within 24 hours. He was maintained on decreasing doses of the steroid for two weeks until the penicillin reaction was anticipated to have cleared. His course was uneventful. No side-effects were noted.

Case 3.—A 53-year-old woman with known severe intrinsic asthma, pulmonary emphysema, and chronic duodenal ulcer was admitted in status asthmaticus. Epinephrine, antibiotics, bronchodilators, oxygen, sedatives, and a slow intravenous drip of iodide with aminophylline were of no avail. An infusion of bovine ACTH produced sudden, severe dyspnea and cyanosis, which responded to intravenously given epinephrine. She slowly responded to large doses of orally given methylprednisolone (28 mg. per day) together with the above medicaments (except ACTH). Melena and moderate epigastric pain occurred on the fourth day of this regimen. X-ray studies revealed no ulcer crater, but chronic deformity of the duodenal bulb was identified and was assumed to be the site of her bleeding. The patient was given a strict ulcer regimen while treatment with methylprednisolone at a dose of 12 mg. per day was continued. Occult blood disappeared from the stool within four days; epigastric symptoms and tenderness were gone within one week. She has been followed up for three months with continued methylprednisolone therapy without recurrence. A modified ulcer program has been maintained.

Case 4.—A 17-year-old male volunteer (as part of the metabolic study) was given 16 mg. of methylprednisolone for one week. He was known to have epilepsy, but he was otherwise in good health. He had not had a grand mal seizure in six weeks, being well-controlled with 100 mg. of sodium diphenylhydantoin given twice daily; this therapy was continued throughout the steroid study. After receiving methylprednisolone for three days, he had a grand mal seizure which lasted about four minutes, and a similar seizure occurred the next day. There were none subsequently. The possibility exists that methylprednisolone precipitated these seizures, since other corticosteroids are known occasionally to do so, as well as producing electroencephalographic changes in predisposed persons.

Case 5.—A 27-year-old man with a nine-year history of chronic ulcerative colitis was found on initial evaluation at the student infirmary to have a typical "lead-pipe" colon that was diffusely friable, bleeding and ulcerated rectosigmoidal mucosa, and pseudopolyps in the sigmoid with a 1-cm. polyp in the descending colon. He was having eight to nine loose stools daily; often these were blood-streaked. Methylprednisolone, 16 mg. per day, was given in an effort to improve his general condition and to permit him to take his doctoral examination before colectomy. Treatment was followed by prompt reduction in the number of stools to one to two a day and symptomatic improvement. After six months he had gained 18 lb. (8.2 kg.), and marked improvement of the rectosigmoid was observed proctoscopically. X-ray examination with use of a barium enema showed no change in either the colon or the polyp. He is at present scheduled for total colectomy with probable ileostomy. This patient experienced many of the typical features of adrenal cortical hyperfunction (Cushing's syndrome): moon face, supraclavicular fat pad, and mild plethora. No other side-effects have occurred.

Case 6.—A 40-year-old man with a 20-year history of chronic relapsing iridocyclitis of unknown etiology awakened one morning with marked tenderness, conjunctival injection, and total blindness in his left eye. Slit-lamp examination confirmed the exacerbation of his iridocyclitis, and he was placed on therapy with 40 mg. of methylprednisolone daily for three days, with gradual reduction in dosage over a two-week period. He noted rapid subjective improvement with prompt loss of pain and discomfort. Some improvement in vision occurred so that he could distinguish light and count near objects within three days after treatment was begun. He remarked that his response to methylprednisolone was unusual in that he did not develop the moon face or other features of adrenal cortical hyperfunction with Cushing's syndrome which he had previously experienced while on similar brief courses of therapy with cortisone or hydrocortisone. No side-effects occurred during the three weeks of therapy.

Case 7.—A 27-year-old man was seen at the student infirmary outpatient clinic complaining of swollen parotid glands of four days' duration. There were no local or systemic symptoms. Both parotid glands were firm and nontender, and the overlying skin was of normal color and temperature. No exudate was present at the duct orifices. There was no lymphadenopathy. The liver was palpable 3 cm. below the right costal margin; the spleen was not felt. A mildly pruritic maculoerythemic rash was present on the pretibial surfaces of both legs. Mumps complement-fixation titer was negative. Histoplasmin and tuberculin skin tests were negative. Chest x-ray revealed bilateral hilar adenopathy with prominent bronchovascular markings. Serum amylase, calcium, phosphorus, alkaline phosphatase, and protein levels were normal. Biopsy of the skin lesions revealed multiple groups of epithelioid cells without caseation and with a mild cellular infiltration consistent with sarcoidosis (sarcoid of Boeck). The patient was given methylprednisolone, 8 mg. four times daily, on March 11, 1958, and by March 25 no parotid swelling remained (see figure). The skin lesions had disappeared within 24 hours, and the liver was no longer palpable after the first week. A chest x-ray taken at two weeks and again in two months showed no significant changes. No side-effects occurred during the course of therapy.

Cases 8-10.—Three patients with severe "thyrotoxic" or "thyrotropic" exophthalmos were treated with methylprednisolone in doses up to 32 mg. daily. All responded favorably and promptly, with rapid reduction in photophobia, lacrimation, and the intense sense of irritation that previously had been present. Rounding of the face and an appearance strikingly similar to that of patients with adrenal cortical hyperfunction with Cushing's syndrome developed at this level of dosage in all three patients. Attempts at reduction of the dosage to avoid these unpleasant effects led each time to the immediate return of the original symptoms. All steroid therapy eventually was discarded, and it was concluded that the hazards of this form of management probably outweigh the benefits and that methylprednisolone does not possess any distinctive advantages over other steroid compounds in the treatment of this condition.

Parotid swelling in patient with sarcoid of Boeck (case 7): *left*, before treatment with methylprednisolone; *right*, two weeks after treatment.

Comment

It is not our intent to imply that corticosteroids are necessarily the treatment of choice for the diseases herein reported. Most of these patients had been on nonsteroidal or other steroidal therapy before methylprednisolone was used. It is to be emphasized that corticosteroids are seldom, if ever, curative and that their use should always be accepted as a "calculated risk." The minimal effective dose should be given over the smallest period of time needed to accomplish the desired response. It is preferable to "get in and out" of steroid therapy if possible. Whenever long-term maintenance therapy is necessary, the physician assumes the responsibility of frequently observing the patient for side-effects and constantly trying to reduce the dose so that serious side-effects are prevented.

Continued modification of the corticosteroid molecule will doubtless produce, in the future, even more potent anti-inflammatory drugs. This can be advantageous to the clinician only if the side-effects can be further minimized and if no new ones are added. It seems highly probable, however, that the major objective manifestations of adrenal cortical hyperfunction are truly the exaggerated physiological effects of the 11-oxygenated steroids of which suppression of inflammation and pituitary inhibition are inseparable parts. If this is true, then further "tailoring" of the molecule may lead to additional changes in the spectrum of biological activity, but always in the direction of a "supercortisone" which still manifests its most important and dangerous metabolic effects. Viewed in this light, there would appear to be an inescapable ceiling on the improvements that are possible in the cortisone-like steroids.

A classification of the side-effects of corticosteroids used in clinical medicine is as follows: This classification is based on the importance of the side-effect to the patient insofar as it is a statistically minor or major risk. Class 1 side-effects are virtually inevitable results of employing suppressive doses as maintenance therapy. The redistribution of fat, striae, acne, excessive hair growth, and plethora reflect an excessive amount of anti-inflammatory hormones present, but when the corticosteroids are truly needed in such doses and for such duration, the cosmetic inconvenience to a patient should not be a serious consideration. All corticosteroids available today will produce class 1 side-effects when given in sufficient doses and for sufficient time.

In class 2 are diabetes mellitus, steroid ulcers, convulsions, thrombophlebitis, hypertension, such mental changes as psychosis, electrolyte disturbances with or without edema, spread or masking of infections, and protein catabolism. These are all potentially major hazards of corticoid therapy. But their infrequency of occurrence, particularly with the newer corticoids, relegates them to a minor role when the patient is not predisposed to any of these side-effects beforehand. Each patient should be carefully evaluated before steroid administration from the point of view of development of these potentially hazardous complications. If the patient is not felt to be predisposed to any of these side-effects, then treatment may be begun, though not with immunity or without continued observations but with a statistically minor chance of producing these complications.

Class 3 side-effects do not preclude the use of corticosteroids, but the greater risk must be recognized, prophylaxis must be employed where possible, and closer observation of the patient is mandatory. With a family history of diabetes, occasional glycosuria, or borderline findings on the glucose tolerance test, the development of diabetes must be recognized as an acceptable risk of steroid therapy. When a patient has a history of peptic ulcer or, perhaps, even chronic epigastric complaints, the use of steroids must be accepted as a class 3 risk. If the benefits still outweigh the possible hazards, an ulcer regimen should be employed concurrently. In epileptic patients the use of the newer, non-edema-producing steroids will probably be attended with fewer steroid-induced seizures. Nevertheless, in treating such a person with steroids, the possibility of inducing seizures should be accepted as a major possible side-effect.

When obese or bedridden patients are treated with steroids, the possibility of thrombophlebitis should be recognized as a potential hazard. Elastic stockings or elastic bandages and ambulation, when possible, should be employed prophylactically. The production of mental changes, including an acute psychosis, during steroid therapy is not a major side-effect in most patients. But, in the emotionally labile, the borderline schizophrenic, and similar persons, steroid-precipitated psychosis must be given serious consideration. Edema formation, electrolyte balance disturbances, and hypertension do not seem to be so frequent with the newer corticosteroids. But, in a patient with preexisting labile or persistent hypertension, the administration of corticosteroids may well cause an exacerbation of hypertension, so that a potential major complication should be recognized before steroid therapy is begun.

It has been our impression that the spread of latent infection or the masking of disseminated infections in patients receiving steroid therapy is not a common occurrence unless the patient is predisposed by underlying serious disease. Special precautions should be employed to exclude latent tuberculosis, which may be reactivated by this form of treatment. In the presence of cirrhosis, carcinomatosis, lymphomatosis, and similar diseases, steroid therapy to the bedridden patient with cachexia is fraught with the hazard of dissemination of infection, and without the patient showing the usual signs or symptoms of the infection. Even prophylactic broad-spectrum antibiotics seem to be of little benefit to such patients. Protein catabolism attends the prolonged use of all currently available corticosteroids. Muscle wasting and osteoporosis is a minor hazard in nonpredisposed patients, but with bedridden and elderly patients or those with cachexia, special attempts to prevent this complication by using gonadal hormones, a high-protein diet, and ambulation should be made.

Chronic hypercortisonism has been reviewed by Slocumb and associates [4] and is produced by prolonged administration of large doses of any of the currently available steroid preparations. The symptoms are increased fatigability, emotional instability, and generalized muscular and joint aching. We have not found chronic hypercortisonism to be a necessary attendant of prolonged administration of suppressive doses of steroids in all patients. Just

how some patients are predisposed to this syndrome is not clear. For the present, the possible production of chronic hypercortisonism as well as diffuse panmesenchymal reactions must be considered a major potential hazard of long-term steroid therapy in some patients. Its presence demands the tedious and slow reduction of the dosage, encouragement of the patient, extra rest, and other measures. All patients receiving significant doses of steroids for prolonged periods of time have secondary adrenal insufficiency as a result of pituitary inhibition. They depend entirely on exogenous corticoids to cope with their daily stresses. This must be recognized as a necessary hazard of steroid therapy before patients are committed to treatment. No predisposition is necessary for this side-effect. All patients receiving significant doses for maintenance therapy must be expected to have adrenal insufficiency. When such major stresses as trauma, infection, and surgery occur, an approximately threefold increase in the dosage of steroids must be employed until the stress has been removed. When steroid therapy is eventually discontinued, this should be done very gradually, and preferably by decrease of the morning doses first, since 70% of the endogenous adrenal cortical output of hydrocortisone is believed to occur between midnight and 10 a. m.[3]

In view of all these side-effects, it is imperative that each patient be evaluated carefully before steroids are employed and that the minimal effective doses be used for the smallest necessary time interval.

The side-effects of methylprednisolone noted in these 77 patients compare favorably with the generally accepted toxicity of prednisone and prednisolone for the doses and the time intervals employed. No unique side-effects were observed. Since the anti-inflammatory effect of this drug has been reported to be 33% greater than prednisolone and 60% greater than prednisone, it appears to be a valuable drug in the medical armamentarium, although continued clinical observation and experience with such a potent drug will be necessary.

Summary

Seventy-seven consecutively treated patients were observed for a period of up to seven months (mean duration of therapy, four and one-half months) while receiving methylprednisolone for various illnesses. The side-effects noted are comparable to those previously attributed to prednisone and prednisolone. No unique side-effects that could be attributed to this drug were observed.

The chief advantage of methylprednisolone seems to be in its enhanced anti-inflammatory effect, while it maintains the relatively low degree of toxicity exhibited by prednisone and prednisolone.

1300 University Ave. (6) (Dr. Gordon).

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PULMONARY OBSTRUCTION.—The control of the trigger factor, such as pulmonary infection precipitating cardiac failure, is of paramount importance. Digitalization, oxygen administration, and other supportive measures should be administered. We should like to warn against the use of opiates and intensive antimony treatment, the latter being toxic to the myocardium. These patients may remain asymptomatic for an indefinite period of time. Increasing knowledge of this condition and the opportunity to diagnose it clinically will enable us to better evaluate the treatment and prognosis of these patients. At present the prognosis is apparently poor once cardiac decompensation supervenes. The governing factor in the short longevity of these patients is the mechanical impairment caused by the irreversible pulmonary arterial and arteriolar obstruction. We agree with other reports that patients with a pronounced increase in pulmonary artery pressure are in a continual danger of death and hence are poor surgical risks.—J. Marchand, M.D., R. A. Marcial-Rojas, M.D., Roberto Rodriquez, M.D., Gerardo Polanco, M.D., R. S. Diaz-Rivera, M.D., The Pulmonary Obstruction Syndrome in Schistosoma Mansoni Pulmonary Endarteritis, *A. M. A. Archives of Internal Medicine*, December, 1957.

EMERGENCY COMMISSUROTOMY IN INTRACTABLE PULMONARY EDEMA

REPORT OF TWO CASES

Hans U. Wessel, M.D.
and
James R. Webster Jr., M.D., Chicago

Acute, intractable pulmonary edema appeared in a patient who was being prepared for mitral commissurotomy. The operation was postponed, and the patient died. There was reason to believe that immediate performance of the operation would have given the patient a chance to survive. Accordingly, in two other patients, with mitral stenosis, who developed pulmonary edema refractory to medical treatment, the operation was done at once. The improvement was immediate, and both patients survived. Since pulmonary edema may set in suddenly during diagnostic procedures or during preparations for surgery, the possible need for emergency commissurotomy must be kept in mind, but it is better to follow the patient closely and to advise surgery before intractable pulmonary edema becomes an imminent threat.

Mitral commissurotomy is usually done as an elective procedure. The patient is operated on after an optimal state of cardiac compensation has been achieved. We first became personally acquainted with the problem of mitral stenosis in which mitral commissurotomy was performed as an emergency procedure because of intractable pulmonary edema in 1955 when a 22-year-old woman was admitted to Chicago Wesley Memorial Hospital for mitral commissurotomy. She gave no history of rheumatic fever. Two years prior to admission she began to have progressive exertional dyspnea, palpitation, and precordial pain with radiation to the left arm and shoulder.

Physical examination, x-ray studies, and the electrocardiogram (ECG) were diagnostic of rheumatic heart disease and mitral stenosis. Right heart catheterization confirmed the clinical impression, showing marked elevation of the right ventricular, pulmonary artery, and pulmonary venous capillary pressures. The cardiac output was diminished and the mitral valve area was estimated to be about 0.5 sq. cm.

The patient was digitalized on admission and taken to surgery three days later. She was given morphine sulfate, atropine, and scopolamine on the morning of surgery. After she had received about 50 mg. of thiopental (Pentothal) intravenously, she suddenly developed acute pulmonary edema. There was marked cough productive of a bloody, frothy sputum, hyperventilation, and wet rales throughout both lungs. The pulse rate increased to 150-200 per minute. A portable x-ray confirmed the diagnosis of severe, acute pulmonary edema. The patient was taken back to her room. Treatment with morphine sulfate, oxygen by mask, and intermittent positive-pressure breathing and antibiotics was of no avail. The temperature rose to 104 F (40 C) rectally. After an initial slight improvement the patient's condition deteriorated rapidly and she died the following day.

Autopsy revealed mitral stenosis with evidence of active rheumatic myocarditis. There was hypertrophy and dilatation of the heart, particularly the right side. Chronic, passive hyperemia was present in the lungs, kidneys, spleen, and liver. The lungs weighed 2,000 Gm. and were quite firm in consistency. Microscopic sections revealed pulmonary edema, bronchopneumonia, and diffuse interstitial fibrosis. Death in this patient was attributed to pulmonary edema and bronchopneumonia. In retrospect it was thought that this patient should have undergone mitral commissurotomy in spite of her precarious condition and that opening of the mitral valve with relief of the obstruction offered the only chance for survival.

During the next two years, we observed two additional patients with mitral stenosis who suddenly developed severe, intractable pulmonary edema. In the first patient this was precipitated by right heart catheterization; in the other by an acute upper respiratory infection. Both patients were operated on during the state of pulmonary edema which medical management had failed to improve. Both patients survived and, in both, relief of obstruction at the mitral valve was almost immediately followed by clinical improvement of the pulmonary edema.

Report of Cases

Case 1.—A 29-year-old woman was admitted to Chicago Wesley Memorial Hospital for cardiac catheterization. She gave no history of rheumatic fever. Seven years before, during labor, she was first seen by a heart specialist and told that she had heart disease. She remained asymptomatic until one and a half years prior to admission. At this time progressive exertional dyspnea, palpitation, and cough began. There were several episodes of hemoptysis. Ankle edema had appeared three months before admission and the patient had been digitalized.

On physical examination she was well developed and nourished. Inspiratory wheezes were heard throughout the lungs. There was no venous distention or abnormal arterial pulsations. The cardiac rhythm was regular at a rate of 90 per min-

From the Cardiovascular Laboratory, Chicago Wesley Memorial Hospital, and the Department of Medicine, Northwestern University Medical School.

ute; blood pressure was 120/80 mm. Hg. The left heart border could be percussed 14 cm. to the left of the midsternal line in the fifth intercostal space. A right ventricular parasternal thrust was felt and a diastolic apical thrill was palpable. There was an apical, middiastolic, low-pitched rumble ending in a presystolic crescendo. The murmur was transmitted to the left axilla and toward the back. The pulmonic second sound was louder than the aortic second sound, and the first sound was loud and snapping over the mitral area. The liver was palpated one finger breadth below the right costal margin. There was no peripheral edema. X-ray showed moderate left atrial and right ventricular enlargement. There was dynamic distention of the main-stem pulmonary artery and minor engorgement of the pulmonary vasculature. The ECG showed right ventricular hypertrophy and strain and sinus tachycardia. Rare fusion beats were observed.

During right heart catheterization the patient developed acute pulmonary edema. The pulse rate increased to 150 per minute and she became cyanotic and extremely restless. Treatment with morphine sulfate, aminophylline, lanatoside Cedilanid C, rotating tourniquets, and oxygen breathing with intermittent positive pressure afforded no improvement. The patient showed only minimal response to subsequent intubation, oxygen breathing, and defoaming with ethyl alcohol mist and venesection. Immediate mitral commissurotomy appeared to offer the patient her only chance of survival.

At surgery, the lungs were of liver-like consistency and showed very little evidence of aeration. The left atrium was entered through the left atrial appendage. No thrombi were found. The mitral valve was so stenotic that no orifice could be felt with the examining finger. A pea-sized mass of calcium was attached to the lateral leaflet near the orifice on a flexible pedicle which hopped up into the atrium during systole and fell into the mitral orifice during diastole. After considerable manipulation, it was possible to finger fracture the match-sized orifice and to dilate it to finger size. This opened the anterior commissure for a distance of 1 to 1.5 cm. During the manipulation, the calcium piece disappeared into the circulation. The carotid arteries were compressed during each manipulation of the valve.

During one of the manipulations the heart went into ventricular fibrillation. Cardiac massage was begun and electrical defibrillation carried out. This threw the heart into asystole. With subsequent massage and injection of calcium chloride into the right ventricle, a normal rate and sinus rhythm was restored after two to three minutes. The patient was given 400 mg. of procainamide intravenously.

The anterior commissure was finally opened for about 2 to 2.5 cm. The posterior commissure could not be opened because of marked shortening and matting of the papillary muscles and chordae tendineae and their fusion with the valve leaflets. At the termination of the procedure the lungs, previously of liver-like consistency, were partially aerated and pink in color. The peripheral portions were soft and pliable and well aerated.

A tracheotomy was performed and the patient's respiration assisted with a Bennett respirator during the day after surgery. The cyanosis cleared within three days and within five days there was no radiographic evidence of pulmonary edema. Nine days after surgery the tracheotomy tube was removed. During the entire postoperative course, the blood pressure remained stable at normotensive levels and the urinary output was adequate. The temperature remained elevated for 10 days. A respiratory alkalosis with hyperpotassemia corrected itself after discontinuation of the respirator. The patient was discharged on the 23rd postoperative day. Maintenance digitalization has been continued. There has been no arrhythmia or decompensation currently (28 months after surgery). She is in functional class 2 according to the American Heart Association classification.

Case 2.—This 49-year-old man was admitted to Chicago Wesley Memorial Hospital on the evening of Feb. 13, 1958, in acute pulmonary edema. He was known to have rheumatic heart disease with mitral stenosis and atrial fibrillation. Two weeks before admission he contracted an upper respiratory infection. He remained at home for five days and received penicillin and symptomatic treatment. On the day of admission, he experienced a return of the chills, fever, generalized malaise, and cough. He left work and went home, at which time he became quite dyspneic. He was brought to the hospital for examination. He had noted no chest pain, ankle edema, palpitation, or sudden gain in weight. On admission, he appeared to be acutely ill and was extremely dyspneic and cyanotic. Blood pressure was 165/115 mm. Hg, pulse 140 and irregular, temperature 101 F (38 C) rectally. His lungs were filled with wet, noisy rales and no heart tones could be heard because of this interference. There was no hepatosplenomegaly and no peripheral edema.

Treatment consisted of oxygen, aminophylline intravenously, rotating tourniquets, venesection, and penicillin. There was immediate improvement, and two hours after admission the chest was clear except for some rales at the right base. With the patient in the left lateral decubitus position, a middiastolic apical murmur could be heard. That evening the leukocyte count was 57,000 per cubic millimeter, with 96% segmented neutrophils, 2% lymphocytes, and 2% monocytes. Nonprotein nitrogen level was 31.5 mg.%; fasting blood sugar level was 107 mg.%, and sedimentation rate (Wintrobe) was 35 mm. in the first hour, with urine normal. An ECG showed atrial flutter with a variable block and an atrial rate of 430. There was also evidence of right ventricular hypertrophy and digitalis effect. A chest x-ray revealed engorgement of the pulmonary vessels with an increased density of the lungs indicative of pulmonary edema. The heart was moderately enlarged with a markedly enlarged left atrium.

He did well for 18 hours after admission. Chloramphenicol was added to therapy because a sputum smear showed a large number of staphylococci. Sputum culture later showed only staphylococci and vancomycin was also given. His color and breathing were good and he rested comfortably during the day. On the next evening the patient once more experienced an episode of pulmonary edema which was again relieved by morphine, aminophylline, oxygen, and rotation tourniquet. However, this second attack lasted considerably longer and was more difficult to control. His temperature rose to 104.6 F (40 C). Even after the acute pulmonary edema had cleared, he continued to have rales and slight dulness at the right base.

On Feb. 15, he once again went into pulmonary edema. This time he was quite refractory to all therapeutic measures previously employed. Meperidine (Demerol) given intravenously and aminophylline temporarily improved his condition. However, he remained in subacute pulmonary edema. Immediate relief of the mitral stenosis appeared to offer the only chance for survival. On opening the chest, it was noted that the lungs had the consistency of liver and appeared to be poorly aerated. Little expansion of the lung could be seen, even with intermittent positive-pressure breathing. The left atrium was entered through the left atrial appendage which contained several thrombi. The mitral valve orifice was located in the posterior third of the valve and was too small to admit a fingertip. Satisfactory opening of the valve was achieved by a commissurotomy knife. By the time the pericardium was closed, the liver-like consistency of the lung had disappeared and the lung appeared soft and well aerated and of a bright pink color. This dramatic change occurred within a few minutes after the valve had been opened. However, blood pressure dropped precipitously and respiration became irregular. Intermittent positive-pressure breathing through the endotracheal tube resulted in improvement and stabilization of blood pressure.

He was returned to his room much improved over his preoperative status. The lungs were appreciably clearer with only a few rales present at the right base. The temperature was 103 F (40.56 C) rectally. During the next few days the temperature gradually decreased, as did the leukocyte count, and the lungs became almost completely clear. The day after surgery the nonprotein nitrogen level was 95%; the creatinine 3.6 mg.% and the carbon dioxide 18 mEq. This azotemia responded to conservative management. He was

discharged one month after admission and 27 days after surgery. At this time the nonprotein nitrogen level was 30 mg.%, the chest x-ray showed no infiltrates, and an ECG showed a coarse fibrillation with a ventricular rate of 80.

Comment

Pulmonary edema in mitral stenosis cannot be explained on the basis of left heart failure. The basic physiological derangement is impedance to blood flow from the lungs due to obstruction at the mitral valve. With a given area, the pressure gradient across the mitral valve is directly proportional to the square of the flow across the orifice.[1] Thus any rise in cardiac output must be accompanied by a rise in left atrial pressure which is transmitted backward into the pulmonary venous, capillary, and arterial system. Theoretically pulmonary edema should occur if the pulmonary capillary pressure exceeds the osmotic pressure of the plasma and the lymphatics are unable to drain the excessive filtrate.

Common precipitating factors are sympathetic stimulation caused by excitement, exertion, exposure to cold, fright, and anger leading to tachycardia and vasoconstriction. Tachycardia results in a shorter diastole with further impairment of left atrial emptying. Vasoconstriction produces redistribution of the blood with its accumulation in the lungs.[2] Robin and Thomas [3] in a study of patients in whom a postmortem diagnosis of pneumonia and pulmonary edema had been made at the Peter Bent Brigham Hospital reported a close interrelationship between these two entities and stated that they frequently coexist and that the occurrence of one predisposes to the development of the other.

Pregnancy in patients with mitral stenosis commonly predisposes to pulmonary edema. Lawler and Gallagher,[4] in a study of mitral stenosis and commissurotomy during pregnancy, reported a rise of cardiac output and blood volume early in pregnancy leading to a 32 to 60% increase above nonpregnant levels by the 28th and 32nd week. This was followed by a moderate decrease until delivery, postpartum rise, and ultimate return to previous levels. Baker and co-workers in 1952 [5] recommended commissurotomy for the treatment of relapsing pulmonary edema, and presented nine patients on whom emergency mitral commissurotomy was performed, with one death. Bailey [6] reported that his patients who had previously suffered from pulmonary edema did well during surgery and had good results. It was his opinion that "history of acute paroxysmal pulmonary edema . . . would seem to urge prompt intervention lest a subsequent attack prove fatal." Bramwell,[7] in a review of the hazards of pregnancy in women with heart disease, spoke in the same tenor when he stated "pulmonary edema is in fact one of the most urgent indications for mitral valvotomy." The same view was expressed by Mulcahy [8] in 1957. He advised emergency valvotomy if pulmonary edema persisted in spite of medical treatment. He reported on 132 cases of heart disease seen during pregnancy within a five-year interval. Of these patients 71 had pure mitral stenosis, 15 mitral stenosis and insufficiency, 15 combined mitral and aortic disease, 9 pure mitral insufficiency, 9 had aortic stenosis or incompetence, and 6 had congenital heart lesions. Seven of these patients underwent mitral commissurotomy because of progressive deterioration. O'Connell and Mulcahy [9] reported an emergency mitral commissurotomy performed because of intractable edema. The patient survived. Another case of emergency mitral commissurotomy during pulmonary edema with survival was reported in 1957 by Dellepiane.[10] The case reported by Krauss and co-workers [11] was a quasi emergency mitral commissurotomy in a woman whose cardiac status had deteriorated rapidly since the fourth month of gestation and she went into pulmonary edema during cardiac catheterization. This patient also survived and had a good result. In contrast, Bramwell [7] saw 11 deaths due to heart failure in pregnancy. In this group were 7 of 16 patients with mitral stenosis who developed pulmonary edema. None of these underwent surgery.

The results of mitral commissurotomy in cases such as ours and those cited above should, as a rule, be good. Good results can be anticipated in patients whose pulmonary hypertension is primarily due to obstruction at the mitral valve, and who are not "protected" against pulmonary edema by secondary precapillary pulmonary arteriolar stenosis and/or chronic right heart failure. Hence, the occurrence of pulmonary edema may mean that a good result will be obtained from surgery, since it requires reasonably good cardiac function for it to develop. However, even though emergency mitral commissurotomy during a state of intractable pulmonary edema affords a fair chance of survival with a good result, it is obvious that operation is preferable before such an emergency situation occurs. Our foremost obligation to our patients with mitral stenosis is to study and follow each one carefully and to advise surgery before pulmonary dynamics make intractable pulmonary edema likely.

1137 Maple Ave., Evanston, Ill. (Dr. Wessel).

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THERAPEUTIC CONTRIBUTIONS OF THE DOCTOR OF PHYSICAL MEDICINE

APPLICATION IN THE CLINICAL PRACTICE OF MEDICINE

Leslie Blau, M.D., Binghamton, N. Y.

The functions of a physiatrist include administration, diagnosis, therapy, and research. For successful therapy it is necessary that he choose modalities, specify times and intensities, make sure of the proper psychiatric approach to the patient on the part of all who administer treatment, and adjust the treatment in general to the needs and responses of the patient. Two case histories illustrate how lesser physical ailments can lead through circumstances to prolonged disability and how physical therapy based on correct diagnosis can relieve the physical condition and rehabilitate the patient. If valuable methods of treatment are not to be misused and neglected, physicians must prepare themselves to use the modern clinical approach offered by physical medicine and to avail themselves of the necessary ancillary services.

In a previous paper the functions of a physiatrist were described.[1] They are administration, diagnosis, therapy, and research. In addition, frequently he has coordinative functions designed to integrate the ancillary services into a central team for successful psychosocioeconomic adjustment of the patient. The role of the specialist of physical medicine as a diagnostician has been elaborated on in detail and supported with a variety of clinical material which clearly illustrated that treating patients with haphazard or tentative diagnoses may lead to poor results or even to untoward consequences to the patient.

A great many factors other than diagnosis deserve serious consideration if we are effectively to attain the desired therapeutic goal. Some of these are the choice of modality, the mode of administration of treatment, dosage, the proper psychiatric approach of those who treat the patient, the patient's inner conflicts, his reaction to the disease, undue prolongation or abrupt interruption of treatments, secondary gains, and, sometimes, even malingering. The purpose of this paper is to explain the reasons why the awareness of these factors is important in the attainment of therapeutic goals and why the clinical acumen of the physiatrist who is usually in charge of therapies is vital and why his services should be available at all times.

Proper Modality

In selecting the proper modality for the treatment of a patient there are a number of considerations. Some of these stem from the effect of the agent and some from the reaction of the patient.

The effect of a physical agent, just like the effect of a drug, can, as a rule, be anticipated. For example, we know that diathermy, infrared lamps, and ultrasonics are heat modalities. Thus, we use them to improve local circulation either by direct heating or by reflex vasodilatation to hasten removal of inflammatory waste products, to allay pain, and to reduce muscle spasm. It should be kept in mind, however, that the random selection of such heat modalities for therapy will result in a great many disappointments not only by poor results but sometimes by deleterious effects to the patient. The reason is that these three modalities develop heat as their principal effect; nevertheless, their mechanism of production, side-effects, and physical characteristics are widely different, creating specific

Medical Director, Rehabilitation Services, Inc.

indications and contraindications that the clinician must keep in mind in selecting them. It may be all right to prescribe infrared heat for many conditions, such as malignancy, osteomyelitis, or postfracture with metallic implants, but diathermy is contraindicated because it may hasten metastasis by its deep penetration, it may have decalcifying effect on the bone, and it will overheat metallic implants.[2] Ultrasonic energy may be a fine modality for many nonparalytic neuropathies, but for others it may be harmful, since it may aggravate weakness as has been shown on animal experiments with electromyography.[3] This discussion could go on not only in regard to these modalities that have been selected to illustrate the point but in regard to all other physical agents, even those as divergent as massage, electrical stimulation, or the many forms of therapeutic exercises.

The other major consideration in the selection of a modality is the reaction of the patient. Here we must think of such factors as general physical condition, age, sex, and individual reactivity. The general physical condition of patients must be considered in prescribing physical treatments; for example, one does not expose a debilitated restless individual to ultraviolet rays because chances are that he may become more restless and irritable. Age is another factor to be considered; hot foot soaks are dangerous in an older person who may have arterial insufficiency in the limbs. Sex also has discriminating limitations; for instance, ultrasonic energy over the lower abdomen of a female patient is not recommended because of the selective sensitivity of the ovaries to this form of physical agent.[3] Individual reactivity cannot be predicted in advance unless the patient's history furnishes such information. An unsuspected individual susceptibility may create uncomfortable situations or even a dire emergency. I remember such a case rather vividly. I prescribed for the patient histamine ion transfer for wry neck. He was in the hospital for a chronic neurological condition, but one morning he woke up with painful, tender muscles in spasm in the posterior aspect of his neck. It is known that histamine as a counterirritant may be helpful, in addition to massage and mobilization exercises, in such a case. He gave no history of asthma, hay fever, or other allergic manifestations. Nevertheless he had individual intolerance to this agent, inasmuch as in 30 to 60 seconds after initiation of this treatment he developed a severe reaction, consisting of generalized urticaria, headache, and feeling of tightness in his chest. It necessitated prompt discontinuation of treatment. He needed epinephrine for relief to prevent a full-blown asthmatic attack. Individual sensitivity is not at all an oddity. A patient, not long ago, had pain in the lower part of her back. As I was taking her history, she found that diathermy was contemplated for her. She immediately stated, "Oh, no! I get a severe headache whenever they give that to me." Peculiarly enough, the attending physician referred her to us with the specific recommendation of diathermy, without knowing the patient's intolerance to it.

Mode of Administration

In the great majority of patients referred for physical medicine and rehabilitation, patients feel the first time that actually something is done for them. Therefore, the environment must be pleasant, safe, and congenial. If, by necessity, unpleasant experiences cannot be avoided, they should be well explained to the patient. This statement is being made with reference to stretching and mobilization exercises. Many patients are referred to physical medicine who suffer from conditions in which pain is the predominant symptom, and the immediate danger is functional loss by keeping the joint in a favorable position. To illustrate my point, I am going to discuss those patients who suffer from rotator cuff syndrome of the shoulder, first described by Codman [4] and more recently by Moseley.[5] These are the patients whose condition had been labeled supraspinatus tendinitis, subdeltoid bursitis, capsulitis, and periarthritis. Years of latent, slowly burning inflammation may be lighted up with an acutely tender, excruciatingly painful shoulder.[6] The patient will be reluctant to move such a joint, which will inevitably result in secondary fixation. The foremost obligation to these patients is to maintain function. A variety of treatments have been advocated for the painful shoulder. Recommendations range from such extremes as to do nothing else but allow the patient simple rest, giving him sedation for pain,[7] to the excision of the acromion for supraspinatus syndrome.[8] In my experience, the best way of treating such patients is to relieve them from pain at any cost to ready them for range-of-motion exercise. During the acute phase, which usually lasts three to seven days, the patient should receive personal attention by the physician. Exercise must be strongly assisted or administered with the patient passively relaxed—never against force. It could be administered as a form of examination or recheck. Preferably, it should be done after the patient has received the most suitable pain-relieving measure, be that local injection of hydrocortisone with procaine, ultrasonic or infrared heat therapy, or short wave diathermy. I feel that x-ray and such toxic drugs as phenylbutazone should be reserved for very stubborn occasional cases, only as the last resort. If motion against gravity is not possible, Codman's test [9] will always succeed to attain 90 degrees or more abduction of the shoulder. A doctor should be available who has the time and clinical competence to spend with such patients, if frozen shoulders are to be prevented.

Dosage

To many people, professional or otherwise, dosage and prescription have no practical connotation in regard to the therapeutic application of physical agents. There is nothing farther from the truth

then the idea that physical agents are always innocuous. It is especially true at this day and age because we use such energies as ultrasonics and microwave diathermy that give relatively little subjective feeling of heat yet heat deep tissues to a considerable degree with a potential danger of damage. The importance of dosage is relevant in regard to other energies used in physical medicine. We exercise a great many patients who are crippled from cardiovascular or respiratory disease and who would suffer from exercise and activity therapies if they were not given dosage according to cardiovascular tolerance and physical fitness.

Psychiatric Approach

The psychiatric aspect of treatment management is that all important, frequently intangible, often ill-understood, and neglected factor of everyday therapeutics which can help or defeat in the attainment of goals. From the first to the last meeting with the patient, the physician must be aware of his *de facto* relationship with him. He must know whether the patient has confidence in him, trusting his professional skill and sincerity. Is the therapist only tolerated by him? The patient's inner conflicts, motives, secondary gains, family relationship, and genuine reaction to his disability must be learned and kept in mind. Since the overwhelming majority of patients have chronic ailments, therapists must have a clear understanding of their goals. Neither undertreatment nor overtreatment can be done. This can be accomplished by precise timing and correlation of results with the attainment of a psychological peak and subjective gratification of the patient. When such a culmination of results is not appreciated, usually an anticlimax follows with precipitation of symptoms, grossly exaggerated by functional overlay. The following cases will illustrate some of these points.

Report of Cases

Case 1.—A 43-year-old woman was referred to me in January, 1957, for opinion and indicated treatment. Her complaint was pain in the lower part of her back since March, 1950, when the following incident took place. She worked as a chambermaid for a hotel; she was moving luggage from one place to another, and, allegedly, she developed such severe pain in her back that she fell on the floor. After about one-half hour, she felt better and cleaned up more rooms. She had to carry luggage again, and she lost consciousness. She was hospitalized for two weeks of rest and heat therapy. Allegedly, x-ray findings were negative. Subsequently, this patient received diathermy to her back three times a week for six years (until October, 1956). She had a thyroidectomy in September, 1951, one and one-half years after the alleged back strain, claiming that she began to be shaky and nervous after the accident.

Examination revealed a paucity of positive findings. She gave a long history while sitting in a chair without showing discomfort. She undressed, favoring her back as she did so. She alleged severe tenderness over the suboccipital, the posterior cervical, and lumbar regions. She moaned and groaned in anticipation of pressure. When she was asked to bend forward, she did so reaching only 20 in. from the floor with her knees extended, saying continuously, "I can't." Results of Faber, Ober, Eli, and straight leg raising were negative, but each maneuver caused her "terrific" pain accompanied by tearless cries. Neurological examination was negative. After the examination she asked her husband to fix her garter and to hand her her clothes, completely favoring her back.

My conclusion was that patient had conversion hysteria. She was a dependent individual, and more physical therapy would have further fixed her disability. Several days later, after consultation with the referring physician, I told her of this opinion. She reluctantly admitted that she had been seen by a psychiatrist, who offered her therapy, but she refused it. At this time she promised to follow through.

Comment.—This case indicates unjustified overtreatment, consisting of six years of diathermy, three times weekly. It helped her to become more dependent, fix her disability, and become virtually a useless cripple. This was a basically unstable individual, who, I believe, with competent guidance consisting of reassurance, motivation, and 6 to 10 physical treatments, could have been channeled back into useful existence.

Case 2.—A 36-year-old woman was referred to me with the diagnosis of torticollis on April 29, 1957, for opinion and indicated treatments. She complained of pain and stiffness in the posterior aspect of her neck, with radiation to her shoulders, of 12 days' duration. She related, also, that the referring physician treated her with oral medication and infiltrated her neck once, seven days prior to her referral. She had not worked since the onset of her pain.

The patient walked into the office holding her head rigidly tilted to the right and flexed; she had round shoulders, and she stooped. She appeared frightened and completely overwhelmed by her disability and also by her husband and mother, who insisted on accompanying her into the examining room. Examination revealed no tenderness. She had normal strength of the sternocleidomastoid muscles. She moved the cervical spine in all directions to almost full range; however, she required a great deal of encouragement to do so. Reflexes in the upper extremities were normal, and there was no sensory change to pin prick. Shoulder and upper extremities were also found normal as to strength and range.

My impression was that the patient had a dependency reaction, being overprotected by her mother and husband. She was without indicated medical guidance, and from a trivial wry neck she developed a conversion reaction. On the basis of this conclusion, I reassured her and gave her, immediately, Sayre sling cervical traction against 2.5 lb. of weight resistance. This was the least amount that gave her the feeling of tension to enable her to relax, permitting cervical rotation movements. This was accomplished without obvious discomfort, and the procedure was followed by ultrasonic, infrared, and massage therapy to relieve her from symptoms of disuse. She left the office as a changed person, cheerfully stating, "I feel much better." Subsequently, she received a total of five treatments under my direct personal supervision. After the third treatment she returned to her job as a cosmetic saleslady.

Comment.—By demonstration of personal interest in this patient, use of kind firmness accompanied by reassurance, indicating that there was nothing seriously wrong with her yet acknowledging that her symptoms were bad enough to cause her discomfort, and use of a few physical treatments, it was possible to prevent the development of conversion hysteria.

Summary and Conclusions

There are many factors that interplay in the attainment of therapeutic goals. Physical energies are often ill applied, and therapeutic results are unsatisfactory. As a result, wrong conclusions are drawn, and a valuable method of treatment is misused or wrongfully condemned. The physician is no longer able to fulfill all therapeutic needs of the patient. Nobody in clinical medicine can escape

the need of ancillary services, and none of us can afford to sacrifice the modern clinical approach offered by physical medicine.

200 Court St.

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SCRAP IRON INTOXICATION

Richard H. Gadsden, Ph.D., R. Ramsey Mellette, M.D.
and
William C. Miller Jr., M.D., Charleston, S. C.

"Scrap iron", an inexpensive alcoholic beverage, is so named because of its peculiar metallic taste. The chief ingredients are isopropyl alcohol and naphthalene. Fifty patients with scrap iron intoxication have been arbitrarily divided into five groups according to their predominant clinical picture. The largest group consisted of patients with acute brain syndrome as manifested by motor restlessness, hallucinations, illusions, extreme apprehension, tremor, and general disorientation. These symptoms, which are identical to those exhibited by a patient experiencing delirium tremens from ethyl alcohol, are usually reversible on abstinence from alcohol. There is a subsidence of most of the symptoms in the patients with toxic psychoses within several days, simply with supportive therapy consisting of use of fluids, vitamins, and sedation or tranquilizers.

From time immemorial man has used alcoholic beverages to deaden psychic and physical pain, to celebrate victories, and to escape from reality. When it has been impossible for men to secure the better alcoholic beverages, they seek, and find, substitutes. With the present price of legally obtainable alcoholic beverages at an all-time high, there is naturally a large market for cheap alcohol and substitutes.

The use of "scrap iron," or "scrap," as some of the users refer to it, was brought to our attention by a marked increase in the number of persons with toxic psychoses who were admitted to psychiatric hospitals. Bizarre physical and laboratory findings were obtained in the study of some of these confirmed scrap iron indulgers; this led to further studies of the patients who used scrap iron and to the toxic effects produced by this concoction.

Investigation into the production or source of scrap iron was not as rewarding as had been hoped. Isopropyl alcohol and naphthalene were identified in the blood specimen obtained from our first patient. Subsequent analysis of his half-full bottle of scrap iron showed isopropyl alcohol and naphthalene in strong concentration. We were greatly interested in determining the reason behind the addition of the naphthalene. The only scientific reason elicited for this addition was the statement of those patients consciously aware that its addition added some "kick to the drink." Obviously, this is a drink of "voltage rather than vintage." It was stated by some of the informants that this alcohol preparation was made in 50-gal. galvanized drums. The base materials are yeast, cracked corn or corn meal, and sugar. Quite often Clorox (a commercial

Assistant Professor of Chemistry (Dr. Gadsden) and assistant psychiatric residents (Drs. Mellette and Miller), Medical College of South Carolina.

preparation used for cleaning purposes) was used as a catalyst in the fermentation. The addition of the isopropyl alcohol (in the form of rubbing alcohol) is made after 48 hours have been allowed for the fermenting of the mash in the drum, at which time moth balls are also added to the mixture. The galvanized drums apparently give the preparation a metallic taste; hence, the origin of the term scrap iron.

Chemical Analysis

Qualitative Analysis.—The qualitative detection of isopropyl alcohol, naphthalene, and beta-naphthol in the urines of patients thought to be consumers of scrap iron was carried out in the chemistry department of the Medical College of South Carolina. The following methods were used.

Ten cubic centimeters of urine was distilled through a water-cooled condenser; the first 5 cc. of distillate was collected. A standard containing small amounts of isopropyl alcohol, naphthalene, and beta-naphthol was treated in the same manner as the sample. The isopropyl alcohol was detected by the method of Brown,[1] the vanillin-sulfuric acid reagent being prepared fresh before each testing period. The presence of naphthalene was detected by the method of Koelsch,[2] with the slight modification of substituting a dilute solution of bromine water for the chlorinated lime solution. This manipulation resulted in no false-negative reactions with the standard solutions and apparently stabilized the color development.

Confirmatory tests for the presence of naphthalene were carried out by the method of Penzoldt.[3] This depends on the formation of a characteristic green color when the naphthalene solution is underlayed with concentrated sulfuric acid. On all urine specimens showing positive reactions for naphthalene, the method of Pellerin [4] was used to demonstrate the presence of beta-naphthol. No quantitative analyses for naphthalene were attempted since detection of beta-naphthol in the urine would indicate ingestion, absorption, and metabolism of naphthalene.

In addition to detecting toxic products in the urine of the patients, we were able to analyze several dozen bottles of bootleg whiskey which had been confiscated by the police department during the several months during which we were carrying out our investigation. Eighty per cent of these bottles revealed the presence of isopropyl alcohol in large amounts, and 60% showed the presence of naphthalene in significant amounts.

Quantitative Analysis.—The chemical methods available to date do not permit the quantitation of a single alcohol in a mixture containing another alcohol or alcohols. In order to obtain analyses for the ethyl and isopropyl alcohol content of scrap iron, we utilized the method of gas chromatography. The Perkin-Elmer vapor fractometer, model 154, was used for these analyses. The column utilized for purposes of fractionation was Perkin-Elmer material F (tetramethylene glycol, dimethyl ether adsorbed on Celite). Sample size was 0.002 cc. Quantitation of the amounts of ethyl and isopropyl alcohols was obtained from standardization of the instrument against mixtures of these alcohols in water. Figure 1 illustrates a standard tracing; Figure 2 represents a tracing of a typical sample of scrap iron containing these alcohols.

Ten samples of scrap iron were subjected to gas chromatographic analysis for isopropyl and ethyl alcohol content. The isopropyl alcohol content was found to be 16.5, 14.6, 18.5, 16.7, 20.2, 15.0, 14.6, 17.5, 24.0, and 25.0% respectively. The ethyl alcohol content was found to be 36.5, 32.4, 46.7, 39.1, 23.0, 38.7, 33.9, 30.3, 32.2, and 34.4% respectively. The maximum error of the method was ±0.3%. All the

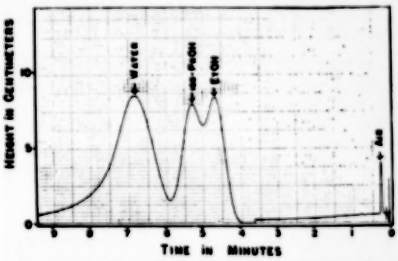

Fig. 1.—Standard tracing of the gas chromatograph of prepared mixture of ethyl alcohol (EtOH; 35%) and isopropyl alcohol (iso-PrOH; 25%) in water.

samples were first analyzed qualitatively for the presence of isopropyl alcohol before being subjected to gas chromatography.

It may be suspected that the most frequently used utensils for the preparation of bootleg whiskey would be galvanized tubs, drums, tubing, etc., because of their relatively low cost and easy availability. During fermentation considerable amounts of acids are produced and may lead to the dissolving of zinc from the containers. Ten samples of scrap iron were subjected to a quantitative analysis for zinc content. For these analyses we modified and adapted the methods of Vallee and Gibson [5] and Hoch and Vallee.[6] The first method gave results of 3.64, 1.02, 1.16, 2.03, 5.14, 0.94, 4.21, 4.36, 1.54, and 2.76 mcg. per liter respectively. The second method gave results of 2.95, 1.22, 1.67, 2.12, 5.07, 1.21, 4.06, 4.09, 1.61, and 2.72 mcg. per liter respectively. The significance of these results is considered later.

Clinical Analysis of Fifty Patients with Scrap Iron Intoxication

The first 50 patients with scrap iron intoxication detected during a three-month period have been arbitrarily divided into five groups according to their predominant clinical picture. The largest group consisted of patients with acute brain syndrome as manifested by motor restlessness, hallucinations, illusions, extreme apprehension, tremor, and general disorientation. These symptoms, which are identical to those exhibited by a patient experiencing delirium tremens from ethyl alcohol, are usually reversible on abstinence from alcohol. There were 26 patients in this group, 15 of whom had complications. There was anemia due to iron deficiency in five, acetonuria (of five days' duration) in one, plastic rigidity in one, diarrhea (of 72 hours' duration) in one, latent syphilis in one, azotemia (with blood urea nitrogen level of 63 mg.%) in one, lobar pneumonia (not aspiration) in three, essential hypertension in one, and cellulitis in one. The average hospital stay was 8.6 days, and there were no deaths in this group.

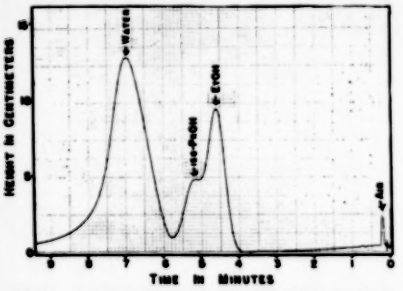

Fig. 2.—Tracing of the gas chromatograph of typical sample of "scrap iron" containing ethyl alcohol (EtOH; 38.7% calculated) and isopropyl alcohol (iso-PrOH; 15.0% calculated).

The second group consisted of five patients with a chronic brain syndrome, but there were irreversible mental changes. There were three patients with medical complications; of these, one had essential hypertension, one had anemia due to iron deficiency, and one had idiopathic epilepsy and anemia due to iron deficiency. Four patients had major psychiatric disturbances which required additional therapy. Two were schizophrenic, one catatonic, and the other paranoid; the third had a severe depressive reaction; the fourth had a case of concussion syndrome resulting from an automobile accident. Three of these four patients were discharged as improved. The catatonic schizophrenic patient died on the eighth hospital day after a pulmonary embolus. Permission for autopsy was refused.

Another group, the second largest, consisted of nine patients classified as having acute alcoholism. Though as a group their hospitalization period was short, their complications were the most severe. One patient fell prior to admission and dislocated the fourth cervical vertebra; this resulted in death on the fifth day in the hospital. Two patients were admitted in severe diabetic coma but recovered and were discharged as asymptomatic on insulin therapy. One patient had congestive heart failure secondary to a myocarditis, the etiology of which we were unable to determine; and, last, a patient in this group remained in the hospital 44 days to recover from an empyema secondary to a bronchopleural fistula.

In any group of alcoholics, gastritis and gastrointestinal disturbances are to be expected. We had two patients with severe gastritis with significant bleeding; one had a moderate hemorrhage and the other a massive hemorrhage. A third patient had a duodenal ulcer with massive hemorrhage. This patient's therapy was complicated by a platelet antigen-antibody reaction which resulted in further bleeding. Also, he had a five-day acute brain syndrome. All three patients were treated with a conservative medical regimen, and there were no deaths in this group.

Last, the most interesting group consisted of three patients admitted in hypoglycemic shock. They were admitted with blood sugar levels of 10 mg.%, 30 mg.%, and 33 mg.% respectively. After an acute episode of hypoglycemia, each of these patients was studied extensively for pancreatic and hepatic disturbances. Complete liver profile studies and cephalin flocculation, sulfobromophthalein retention, dye excretion, total and fractional protein level, prothrombin time, and glucose tolerance curve determinations were done. No abnormalities were found. Although we were familiar with the literature pertinent to hypoglycemia associated with bootleg whiskey, we did not suspect Solox (a shellac and paint solvent consisting primarily of ethyl alcohol and methanol) as the toxic agent, because the patients denied the ingestion of this fluid, and we were unable to detect methanol in either the blood or urine. However, one year later we were able to trace a similar case of hypoglycemia to Solox ingestion because of the telltale presence of methanol in the urine and blood of this individual. Undoubtedly these first three cases of hypoglycemia were likewise due to consumption of Solox. This emphasizes the point originally shown by Tucker and Porter [7] that the hypoglycemic effect of Solox is delayed. In our first three patients the metabolism of the methyl alcohol component of Solox was completed before the hypoglycemia occurred. This experience also illustrates the time-honored maxim that bootleg whiskey is often a mixture.

Toxicity

We were rather surprised at the scarcity of articles pertaining to case reports, toxicology, and symptoms of isopropyl and/or nephthalene poisoning in adults. The following symptoms and signs were compiled from several books on toxicology. Ingestion of isopropyl alcohol [8] results in dizziness, nervous and muscular disturbances, headache, marked fall in blood pressure, gastrointestinal hemorrhages, hypotension, shock, coma, uremia, and anemia. Ingestion of naphthalene [9] results in gastrointestinal irritation, diarrhea, liver and kidney damage, anemia, depression, convulsions, jaundice, and coma. No mention of the frequency of toxic psychosis was found in the articles that we reviewed, but in this series of 50 patients a significant majority exhibited definite symptoms of an acute or chronic brain syndrome out of proportion to the quantity of alcohol consumed.

More literature relevant to the toxic effects of naphthalene was found than articles reporting isopropyl alcohol toxicity. It is repeatedly emphasized in the literature that there is an individual susceptibility toward the toxic effects of naphthalene. Fifty years ago this product was frequently prescribed for the treatment of certain enteric fevers, namely typhoid, with only an occasional severe side-effect being recorded. The majority of the case reports relating to the toxic effect of naphthalene were concerned with the cumulative effect of naphthalene and the subsequent course of the patient who experienced a hemolytic anemia. Heretofore this has been reported primarily in children.

Smillie [10] reported four cases (three adults and one 10-year-old boy) of severe hemolytic anemia with the use of beta-naphthol for therapy of intestinal ancylostomiasis (hookworm) and concluded that it represented an individual susceptibility to the drug. In a report by McGregor,[11] we found references to three other cases of hemolytic anemia in adults, associated with the ingestion of moth balls. We had two such cases (to be reported in a later paper) not included in our first 50 cases. The hemolytic anemia was manifested by normochromic normocytic anemia with jaundice and elevated bilirubin and increased urobilinogen levels. Both patients reverted to normal on iron therapy and abstinence from scrap iron. Although we did not conclusively prove naphthalene, rather than isopropyl alcohol, as the toxin by challenge dosages of naphthalene, it is a fair assumption on the basis of these previous reports and the demonstration of beta-naphthol in their urine. The mechanism of this acquired hemolytic anemia is thought to be a congenital defect of glutathione in the red blood cells.[12]

Burning sensation in the urethra on urination was reported in the literature; however, this symptom was not obtained from any of our patients whose urine was positive for naphthalene. No gross or persistent microscopic hematuria which would suggest genitourinary pathology was noted in our series. Although the duration of the ingestion of scrap iron could not be determined in our patients, these latter two ascribed symptoms have been found mainly in people who have had prolonged contact with naphthalene. Likewise the known carcinogenic peculiarity of bladder cancer is known to exist only in workers in moth ball factories—we had no such cases.

McCord and associates,[13] in 1948, reported three cases of isopropyl alcohol intoxication and a review of the literature in regard to its toxic effects and reported: "Little is known about the effect of isopropyl upon the human individual other than some reports in the German literature in which small amounts of alcohol were taken experimentally by mouth." We did not notice the bradycardia or fall in blood pressure which has been reported, but rather an elevation of blood pressure and tachycardia. These two symptoms may be related to the delirium which many of the patients were experiencing at time of admission to the hospital. Animal experiments have shown that isopropyl alcohol is approximately twice as toxic in all respects as ethyl alcohol.[14] This was borne out in our case histories. Few patients were able to ingest more than one-half pint of scrap iron in six to eight hours and remain conscious. Only chronic alcoholics could drink as much as one pint and remain conscious. As reported by McCord and associates,[13] the blood level of isopropyl alcohol for drunkenness is 0.050 Gm.% and coma at 0.075 Gm.% in contrast to that of ethyl alcohol, which is more than twice these values.

We were able to find in the literature one case of isopropyl alcohol ingestion in an adult. The clinical picture was similar to that in our cases of acute brain syndrome, but the patient had the additional complications of lower nephron nephrosis which responded rather quickly to a conservative medical regimen. Our one case of azotemia (blood urea nitrogen level, 63 mg.%) was secondary to dehydration and responded quickly to hydration.

It was suggested that the metallic taste of scrap iron might represent the presence of zinc in a significant quantity; however, the amount found in representative samples of this fluid is comparable to the quantity present in the local drinking water. There were no symptoms which could be attributed to zinc toxicity alone. The metallic taste is probably caused by the strong concentration of alcohols and, perhaps, heavy metals in trace quantities.

Isopropyl alcohol is thought to be converted in the liver largely into acetone, which is excreted as such by the lungs and kidneys. This was borne out in only one patient, who had acetonuria for four days, of the 50 patients who were known to have drunk moderate amounts of isopropyl alcohol.

Naphthalene likewise is broken down in the liver into beta-naphthol, phenol, and muconic acid. All are excreted by the kidneys.

There is nothing of significant note in the treatment of our patients. There was a subsidence of most of the symptoms in the patients with toxic psychoses within several days simply with supportive therapy consisting of use of fluids, vitamins, and sedation or tranquilizers.

Summary

A new term, hitherto unknown to us, has become prevalent among imbibers of other than legally obtained alcoholic beverages. This term is "scrap iron" and is named thus because of the peculiar metallic taste. The chief ingredients are isopropyl alcohol and naphthalene. It is felt that the consumption of this preparation could become more in evidence because of the cheapness (isopropyl alcohol recently being sold in a large store for nine cents a pint) and because of its intoxicating effect. The frequency of severe physical and mental symptomatology was reviewed. It is anticipated that prolonged drinking of "scrap iron" will produce qualitative and quantitative effects similar to those of ethanol but of a more severe degree in a shorter period of time. As yet we have not observed the cumulative effects of scrap iron in a patient. Further investigation is warranted into the toxic effects, and steps should be taken to hinder the sale of these toxic substances.

16 Lucas St. (Dr. Gadsden).

Dr. Peyton C. Teague assisted in performing the quantitative analyses of scrap iron in this study.

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CLINICAL NOTES

ARTERIAL THROMBOSIS WITH GANGRENE AFTER USE OF PROMAZINE (SPARINE) HYDROCHLORIDE

Morton Opinsky, M.D., A. Frederick Serbin, M.D.
and
Joseph E. Rosenfeld, M.D., Hartford, Conn.

This paper is a report of two cases of unusual and remarkably similar complications resulting from intravenous injection of promazine (Sparine) hydrochloride. Promazine, a phenothiazine derivative, is recommended in treatment of anxiety states, somatic disturbance, alcoholic syndromes, drug addiction, psychosis, manic depressive states, and schizophrenia.

Many side-reactions have been reported with its use, some mild and some severe. Untoward and catastrophic vascular complications in the two patients with alcoholism reported on here followed intravenous injection of this drug.

Lemere,[1] in 1950, warned that further observations are needed to establish the exact role of promazine therapy in intoxicated alcoholics. He

reported that in one patient, after several intramuscular injections, promazine caused such a severe local reaction, with marked inflammation and induration at the site of injection, that its use had to be discontinued. He also reported three instances of convulsions after intramuscular administration of promazine in severely intoxicated patients. He felt at that time that these convulsions may have been either simply coincidental effects of withdrawal of alcohol or results of inadequately sustained tranquilization from two widely spaced subsequent doses of promazine. He also stated that other alcoholics refused to accept further intramuscular medication with promazine during the initial sobering up phases of their treatment because it made them worse.

In this report of two cases of vascular complication after intramuscular injection of promazine, it would seem more than coincidence that two cases so parallel in symptoms should follow each other within a few weeks. When the millions of intravenous injections of drug solutions that are given each year without mishap are considered, it is significant that two cases of arterial thrombosis after the use of the same drug can be reported from one community. For this reason, these experiences are related so that caution may be observed in the further use of promazine. In both cases, promazine was used for its tranquilizing effects after the heavy use of alcohol.

Report of Cases

Case 1.—A 37-year-old woman was given 25 mg. of promazine in the left antecubital vein for tranquilization after the heavy use of alcohol. The patient was uncooperative and in a state of extreme agitation. After the needle had penetrated the vein and a small amount of promazine had been given, she jumped and then complained of severe pain in her hand and fingers. The needle was withdrawn, and her fingers and hand became cyanotic. She complained of intense pain at the site of injection. Immediately, procaine hydrochloride was injected into this site to alleviate the local pain. The pain, however, persisted, and stellate ganglion blocks were performed without relief of cyanosis or pain. Within a few days all the fingers of her left hand gradually became mumified, and dry gangrene ensued. This extended to the flexion crease of the wrist. No pulses were present at the elbow or the wrist. Four weeks later, on Dec. 19, 1956, an exploration of the antecubital fossa was done and the terminal portion of the brachial artery was found to be markedly constricted and of ropy consistency. It was totally occluded for a distance of 1½ in. There were no pulses through the cord-like structure, but, when the artery was opened, there was a slight flow of blood coming back through the radial and ulnar arteries. A polyethylene interval graft was inserted at the distal end of the viable brachial artery. This did not alter the clinical appearance of the hand. On Dec. 26, 1956, an amputation through the lower third of the forearm was performed. There was little bleeding, except for a weak flow through the dorsal interosseous artery. The wound healed subsequently without further complication. The patient continued to do well except for some pain in the arm stump; this pain ultimately subsided.

Case 2.—A man, aged 28, was seen on Feb. 2, 1957, at the McCook Memorial Hospital. He had been given an intravenous injection of 25 mg. of promazine approximately 48 hours previously. The injection was given in the antecubital vein of his left forearm. On receiving the injection, the patient was said to have moved and to complain of pain in his hand. He later showed cyanosis of the distal phalanx of the ring finger and coolness of the whole ring finger. There was much pain on movement of his finger. The remaining portion of the hand appeared normal. There were also several irregular cyanotic blotches extending down the volar aspect of the forearm, distal to the site of injection. The areas measured from about 4.5 cm. in the upper aspect of the arm to 1.5 cm. in the lower arm. These areas were very tender. A radial pulse was present and in good force. A brachial plexus block and stellate ganglion block were done, and the cyanosis in the finger and the blotchy areas on the forearm returned to a normal color. Immediately after these procedures, the ulnar pulse became weakly palpable. Exploration of the antecubital fossa in the region of the injection was done and an area of thrombosis, 2 cm. long, in the left ulnar artery was found. No site of perforation of the artery could be found. No grossly abnormal findings could be noted in tissues at the site of injection. The artery was opened, but the clot seemed to be closely adherent to the arterial wall and could not be removed easily; thus, it was decided to excise the ulnar artery at the thrombosed portion of the artery. All other arteries seemed patent. A periarterial neurectomy of the distal brachial artery and its branches was done. After the operation, cyanosis in the distal phalanx and the blotchy areas on the forearm became more pronounced. The patient was treated with continuous stellate ganglion blocks for several days without any change. Heparin was also given. Pain continued in the distal phalanx, with progressive gangrene, and partial amputation of the finger was done on March 4, 1957. The blotchy areas on the forearm broke down but eventually healed. Several months later, a left dorsal sympathectomy was done at another hospital for pain and coldness in the hand. After the sympathectomy the pain and coldness in the hand was relieved.

Summary

It is felt that the etiology of the arterial spasm and thrombosis in two alcoholic patients treated with promazine (Sparine) hydrochloride might well be due to infiltration of the promazine into the soft tissues or reflexly through vein irritation after the intravenous injection. Extension to branches of the brachial artery causing gangrene in the hand, as reported in the first case, and gangrene in the left ring finger, in the second case, may have been by this mechanism. It is suggested that promazine be used intravenously with caution or perhaps not at all via this route.

179 Allyn St. (3) (Dr. Opinsky).

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SUBUNGUAL HEMORRHAGE IN PAN WASHERS

PRELIMINARY REPORT

Peter I. Long Jr., M.D., Dayton, Ohio

A great many articles [1] have been written concerning the effect of soaps and detergents on the hands, especially since the widespread introduction of detergent cleansing agents. To my knowledge little information has been obtained on the effects of detergents on the nails and nail beds. Viecelli [2] reported a case of onycholysis on exposure to alkalies in 1936. My attention was directed to this matter by the occurrence of three cases of nail-bed disease in pan washers on the dietetic service of the Veterans Administration Center. The cases reported here varied in intensity from a mild soreness of the nails to extensive subungual hemorrhage.

Report of Cases

CASE 1.—A 61-year-old male presented with the complaint of very sore and tender nails. Examination revealed numerous small hemorrhages under all the nails of both hands (fig. 1). The lesions were noted primarily under the distal two-thirds of each nail. The skin of the hands was dry, and there was erythema over the joints. A complete physical examination was normal. There were no hemorrhagic lesions elsewhere on the body. The laboratory findings were as follows: The white blood cell count was 5,700 per cubic millimeter, with 70% polymorphonuclear leukocytes, 24% lymphocytes, 5% monocytes, and 1% eosinophils. The red blood cell count was 4,800,000 per cubic millimeter, and the hemoglobin level was 12.8 Gm. per 100 cc. The patient's bleeding time was 1½ minutes; the platelet count was normal. The coagulation time was 15 minutes, the prothrombin time 63%, Coombs' test negative, and the serology negative. The patient's chest x-ray was normal.

The man's history revealed that he had been employed for three weeks as a pan washer. His nails became sore during the second week of employment. There was no previous history of sensitivity to soaps or detergents, nor was there any familial history of blood dyscrasia.

These hemorrhages progressed to a point that paracentesis of one nail was necessary to relieve the pressure symptoms. Over a period of two months the lesions became chronic in nature and the distal portion of the nails was separated from the nail beds. However, no nails were lost, and the patient's nails healed on his removal from the pan-washing job.

CASE 2.—This 65-year-old male came to the first-aid room for treatment of a minor laceration of his hand. During treatment, he complained that the fingernail of the right fourth finger was sore. Examination revealed a subungual hemorrhage beneath this nail (fig. 2*A* and *B*). He could not remember any trauma to the nail. In approximately one month's time the man was seen again, and a chronic lesion involving one-third of the nail had developed: The distal portion of the nail was separated from the nail bed. The nail itself was dark and brittle. A complete physical examination was normal. The man's history noted that he had been working as a dishwasher for a year but had been transferred to the pan-washing room two weeks prior to the onset of his nail trouble. The laboratory findings were as follows: The patient's white blood cell count was 7,300 per cubic millimeter, with 72% polymorphonuclear leukocytes, 20% lymphocytes, 7% monocytes, and 1% eosinophils. His blood coagulation time was 11 minutes, and his platelet count was normal. Coombs' test was negative. Results of serologic studies were negative. His chest x-ray was normal.

CASE 3.—A 21-year-old male reported sore fingernails two weeks after being hired as a pan washer. There were numerous small hemorrhages under the distal one-third of the nails, and the nails were extremely tender on pressure (fig. 2*C*). The physical examination was otherwise normal. The laboratory findings were as follows. The white blood cell count was 5,750 per cubic millimeter, with 35% neutrophils, 29% lymphocytes, 12% monocytes, 2% eosinophils, and 2% basophils. The hemoglobin level was 13.2 Gm. per 100 cc., hematocrit was 44.5 vol. %. The patient's bleeding time was 2½ minutes; his coagulation time was 10 minutes; and his platelet count was normal. Coombs' test direct and indirect, was negative; the results of serologic studies were negative. His chest x-ray was normal.

Comment

At this institution there are three separate pan-washing rooms located in various sections of the hospital. In each of the pan-washing rooms the same water supply, detergents, and steel wool are used. The same types of utensils are used everywhere. During the interval between the discovery of the first and third patient, the type of detergent cleansing agent was changed from a powdered detergent to a liquid detergent. However, the lesions developed while each of the detergents were in use.

All three cases of subungual hemorrhage developed in one pan room. The only difference in the pan-washing procedure that could be discovered was that our three patients all used heavy rubber gloves while working. All other pan washers either wore no gloves or only light cotton gloves to protect their hands from the steel wool.

We observed the washing techniques of the patients and found that during the course of the washing each patient accumulated 50 to 175 cc. of the washing solution in their gloves. The pH of the washing solution in the sinks was tested on a standard pH meter, and it varied from 7.1 to 10. The water temperature varied from 100 to 112 F. In the gloves, the pH of the washing solution

From the Veterans Administration Center.

varied from 5.2 to 6.7. The glove solution temperature ranged from 100 to 104 F. Each patient was patch tested with each of the two detergent solutions and with rubber from the gloves without reaction.

The explanation of the mechanisms of these hemorrhages presents an interesting problem. Several factors stand out. First, the pan scrubbing is fairly traumatic, entailing a lot of hard scouring, and this would have a tendency to separate the nail from the nail bed, traumatizing the subungual tissue. Second, only the men who wore gloves developed this lesion although they demonstrated no sensitivity to rubber. Third, the pH of the washing solution trapped in the glove was more acid than that in the washing sinks. This may be accounted for by perspiration and the action of the keratin on the pH of the detergent solution as noted by Martin-Scott and Ramsay.[3]

It is interesting that only men who had been employed as pan washers for a short period of

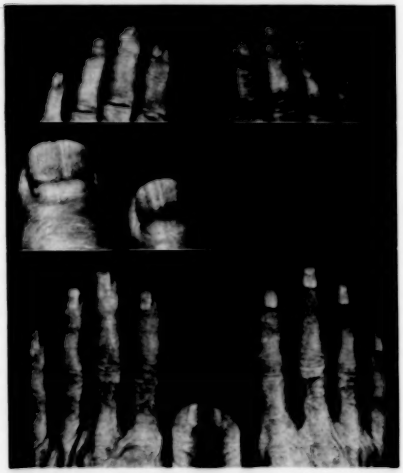

Fig. 1 (case 1).—*Top*, subungual hemmorrhage after three weeks' exposure to pan washing. *Middle*, maximum extent of disease. *Bottom*, four months after removal of patient from job as pan washer.

time developed these lesions. The fact that they were not accustomed to this type of labor may be an important factor.

In determining the exact pathogenesis we must consider whether these lesions are purely traumatic or whether we are dealing with some toxic factor as well. Pure trauma seems unlikely since I feel the lesions would be more common if this were the circumstance. The change in the pH of the detergent solution trapped in the glove to the acid side may cause the breakdown of the detergent, with the subsequent release of a more irritating substance in

Fig. 2.—*A* (case 2), subungual hemorrhage limited to two nails of right hand. *B* (case 2), after three months' continued exposure to pan washing. *C* (case 3), small subungual hemorrhage after two weeks of pan washing.

the form of a sulfonic acid. This possibility is being investigated at the present time. Regardless of the exact pathogenesis, the subungual lesions I have described present a problem of medical and legal significance, since the cosmetic and functional impairment may be severe.

Conclusions

Three patients had subungual hemorrhage. All of them were pan washers using detergents and rubber gloves in the washing process. The subungual hemorrhages subsided and the lesions completely cleared on removal of the patients from their jobs.

A change in the pH of the detergent solution trapped in the gloves and the trauma associated with scrubbing appeared to be the primary etiological factors. Further study is indicated to determine the exact pathogenesis. Prompt recognition of the lesions and elimination of the offending agent is necessary to prevent extensive nail bed damage.

4100 W. Third St.

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MAMMARY CARCINOMA

WHEN a patient presents herself with a mammary carcinoma that has obviously metastasized distantly, or when recurrence with metastases occurs after mastectomy, treatment varies somewhat depending on whether the patient is in the age group from premenopausal up to 5 years postmenopausal, or more than 10 years postmenopausal, with a borderline or transitional period of about 5 years between. In the former group oophorectomy is recommended by many, but since this is only effective in 30 to 40% of patients Slaughter [3] recommends irradiation of localized metastases, particularly those in weight-bearing bones, which he claims is effective in about 90% of such patients. In almost 50% of these patients the tumor is hormone-dependent [4] and in most of this group after ovarian ablation a remission averaging about nine months is observed. If there is no response to oophorectomy the patient probably will not respond to adrenalectomy, but in patients with hormone-dependent cancer adrenalectomy may result in a second remission of about the same average duration.

Because the results after oophorectomy and adrenalectomy are usually short-lived, attempts have been made to get the same results without operation," but so far the achievement of "medical adrenalectomy" has not been realized. Subjective improvement after the giving of prednisone or prednisolone is often dramatic but rarely prolonged. The drugs are especially useful in getting patients in better condition for oophorectomy or adrenalectomy, and in treating patients with cerebral metastases, hypercalcemia, and lymphedema.[4] Objective evidence of improvement after this form of treatment has been observed in electroencephalograms in patients with cerebral metastases.[6] Kennedy [10] found that fluoxymesterone is as effective as testosterone and has the advantage that it can be given by mouth. If in the latter group there is no response, they switch to estrogens and in the frankly postmenopausal group they give estrogens routinely.

One other form of endocrine ablation, hypophysectomy, has been used as a last resort. This heroic procedure is most successful in patients with hormone-dependent tumors but it is definitely contraindicated in fragile old women worn out by long-continued x-ray and hormonal treatment. Other contraindications are a history of cardiovascular disease, multiple painful rib fractures, massive pulmonary metastases, respiratory paralysis due to cord lesions, and evidence of hepatic insufficiency or renal damage in some patients. Lawrence [11] describes a procedure whereby pituitary activity can be abolished by proton irradiation. Patients so treated had remissions lasting as long as 20 months. Illingsworth [12] states that the results from adrenalectomy and hypophysectomy are not significantly different. Adrenalectomy is technically a much simpler procedure. Proper selection of patients for either operation is still difficult. After any type of endocrine ablation relapses occur. This is interpreted to mean that aberrant endocrine cells not removed at operation have undergone a compensatory hypertrophy or that the cancer is composed of a mixture of cell types of varying hormonal dependence and that after suppression of the hormone-dependent cells the hormone-independent cells continued to grow. He concludes that endocrine treatment should be tried earlier in the course of the disease than has been the practice.

In discussing chemotherapeutic agents for mammary carcinoma Taylor [13] states that conclusions as to their value are fraught with uncertainty because of the variable natural course of the disease, variations in the selection and size of samples used by different observers, the difficulty of measuring regression of the disease objectively, and the difficulty of attributing regressions to the procedure being tested rather than to late effects of the previous treatment or other factors. He based this particularly on the inconclusive results of treatment with

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triethylenethiophosphoramide (Thio-TEPA). More recently Moore and Pickren [14] reported that a few months of palliation may be obtained by using triethylenethiophosphoramide. The chief importance of this observation is that it serves to keep up interest in chemotherapeutic research. It is hoped that a derivative or closely related preparation will be found that will surpass any chemotherapeutic agent used thus far.

The diagnosis of mammary carcinoma at an early stage still offers the best prognosis. Although in patients with this disease the die is largely cast by the tumor-host relationship which determines the number of patients curable by any form of treatment, the patient should be given the benefits of the best treatment available. As in few other forms of cancer, treatment must be individualized. A fixed plan of treatment is the refuge of the intellectually destitute.

DUMPING SYNDROME

One of the most unpleasant sequelae of gastric surgery is the complex physiological response to the presence of undigested food in the jejunum commonly called the dumping syndrome. It plays a role in postoperative weight loss and is a major factor in patients' dissatisfaction with the results of gastrectomy. Much confusion has arisen over the exact diagnostic criteria of this syndrome. Everson and co-workers [1] consider it a vasomotor phenomenon characterized by weakness, sweating, or dizziness. If any one of these symptoms occurs during or within one hour after eating, a positive diagnosis can be made. Although some authors speak of the nausea and vomiting that often accompany the syndrome these symptoms are an unreliable indication of true dumping syndrome.

According to Jordan [2] the incidence of the syndrome varies from 2 to 45% of patients who have undergone some type of subtotal gastrectomy. He attributes this discrepancy to the fact that those whose symptoms depend on the ingestion of certain foods may be erroneously diagnosed as having a food intolerance rather than dumping syndrome. Everson states that if only severe symptoms are considered the incidence is low and may even approach zero in some series. If on the other hand patients whose only symptoms are epigastric fullness and nausea are included an erroneous incidence approaching 100% may be reported. The fact that leading questions must be asked, because even patients with true dumping syndrome often do not complain of their symptoms, makes it hard to arrive at an accurate estimation of the incidence. Jordan believes that only about 15% have symptoms of sufficient severity to require treatment. No clear-cut increase in the incidence of dumping syndrome was found to be associated with an increase in the proportionate amount of stomach resected but the incidence did decrease with the elapsed time after operation. In other words many patients adjusted to their symptoms in time so that even though the symptoms did not disappear they became less troublesome.

Theories as to the underlying cause of dumping syndrome can be divided into mechanical and physiological.[3] According to the first, rapid emptying of the stomach causes symptoms by overdistending the jejunum. The weight of the distended jejunum causes traction on the stomach and this may be an added factor. Operative procedures with these factors in mind have been tried and good results have been reported by enthusiasts but the fact that dumping syndrome may be observed in the absence of these factors would indicate that they are at least not the sole cause. Suggested physiological factors that may cause dumping syndrome include hypoglycemia, sideropenia, altered digestion of fats, adrenal stimulation, fall in serum potassium level, and a drop in blood volume. No proof that any of these is the true cause has yet been produced. Webber and co-workers [3] found that in most patients with dumping syndrome there is a decrease in both blood volume and the potassium level but no correlation between this and the patient's symptoms was observed. Poth [4] states that dumping syndrome can be induced in anyone by introducing a large enough amount of hypertonic solution into a large enough portion of the small intestine and that the symptoms are not due primarily to distention but rather to depletion of extracellular fluids. Although the symptoms of dumping syndrome are almost identical with those of hypoglycemia the time relation to food taking is different. Hypoglycemic symptoms do not occur until two to four hours after eating.

The treatment of this condition was recently discussed in these pages by Jordan. Failure to control the symptoms by the use of a judicious diet, avoidance of fluids at meal times, rest after meals when convenient, and parasympatholytic drugs is rare. Although fluids should not be taken with the meals, as soon as symptoms occur the patient should drink 250 to 500 cc. of any fluid containing no sugar or electrolytes. Poth believes that gastrectomy should be combined with the construction of a gastric pouch (using a portion of the jejunum) of sufficient volume to act as a reservoir. His patients have not been followed long enough for the final outcome to be evaluated but the results judged by a short-term follow-up appear promising. In any case an increase in the knowledge of the pathogenesis of this condition should provide leads for further improvement in present methods of treatment.

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ORGANIZATION SECTION

PRELIMINARY GUIDE FOR MEASURING WORK ABSENCE DUE TO ILLNESS AND INJURY

The following Preliminary Guide for Measuring Work Absence due to Illness and Injury has been prepared by the Committee on Medical Care for Industrial Workers, a joint committee of the Council on Medical Service and the Council on Industrial Health, for those physicians who are concerned with this problem in their practice of medicine. Reprints of this article are available on request either to the Council on Medical Service or the Council on Industrial Health. It is the hope of the two councils that physicians who are dealing with various aspects of the problem of work absence will review this guide and submit any suggestions they may have for its future revision.

The subject of work absence among the employed population has occasioned considerable concern in medical, management, labor, and government circles and in various community organizations. Over the years, an appreciable body of literature has been developed in the United States dealing with medical, economic, and sociological aspects of this problem. Each such contribution, while helping to explain the nature of segments of the problem has, at the same time, led to some confusion through presenting differing definitions, measurements, and attitudes towards absence.

In an effort to delineate one of the most important areas of work absence, namely, absence due to illness—whether confirmed by the physician or not—and injury (hereinafter referred to as "sick absence"), the Committee on Medical Care for Industrial Workers, a joint committee of the Councils on Medical Service and Industrial Health of the American Medical Association, has drawn upon many resources to develop recommended guides for defining and measuring such morbidity absence. The use of uniform definitions and measurements in the maintenance of sick absence records will insure comparability of such records not only within a given industry from one period of time to another, but also between different industries. It is hoped that all health personnel engaged in the collection of such data and management will adopt the Committee's recommendations so that a clearer recognition of sick absence and a more accurate evaluation of its real impact upon industry and the employed population may result.

The Committee on Medical Care for Industrial Workers recognizes that established company practices may, in some instances, present an obstacle to the adoption of these preliminary guides. It is convinced, however, that uniform information such as that called for in this guide, and in forms based thereon, can be secured as well as such additional information as individual companies feel is necessary. Future experience will determine the extent to which this guide should be modified, and how the information gathered over a period of time among many industries can best be compared and put to practical use.

Identifying and Measuring Work Absence

Definition.—An employee absent from work should be considered to be on "sick absence" when the reason for absence is his or her own illness or injury. The total duration of such an absence is to be considered as "sick absence" and recorded accordingly. The practice is to be discouraged of giving to an absence, which by this definition is sick absence, some such label as "annual leave," "administrative leave," or "leave without pay," after the absence has exceeded a specified number of days, in order thereby to avoid the recording of this as a sick absence. Maternity leave should not be classified as sick absence, except when complications increase the normal maternity leave.

Classification.—The definition recommended is based upon a distinction between absences due to, and those not due to, illness or injury. Sick absence, i. e., that due to illness or injury, is further classified as non-occupational or occupational in origin. An occupational sick absence is one that arises out of and in the course of employment.

Classification Divisions.—Classification divisions are (*a*) nonoccupational illness, (*b*) nonoccupational injury, (*c*) occupational illness, and (*d*) occupational injury.

Basic Measures of Sick Absence.—Severity rate, frequency rate, and disability rate (all defined below) are the three measures which have been selected to promote uniformity in the collection, recording, and interpretation of sick absence statistics. Although other measures are in use and uti-

lized for different purposes and reasons by various companies, the use of these three measures is recommended as standard practice. The Committee further recommends, for denoting duration of absence, the use of calendar days rather than "scheduled days" or work days," since calendar days in industrial usage is nearer the correct duration of disability from an illness or injury. This is in line with the practice used in connection with sickness disability benefit payments, and in sickness surveys conducted among the general population.

Severity Rate: Severity rate is defined as the number of calendar days lost per absence. The formula is as follows:

$$\frac{\text{No. of calendar days of absence due to nonoccupational illness (or injury)}}{\text{No. of absences due to nonoccupational illness (or injury)}}$$

Frequency Rate: Frequency rate is defined as the number of absences per 1,000 employees per unit of time (month or year). The formula is as follows:

$$\frac{\text{No. of absences due to nonoccupational illness (or injury) per month or year}}{\text{Av. no. of employees on payroll}}$$

It is recommended that "average number of employees" be arrived at by taking an average of the totals of employees on the first and final pay days of the month.

Disability Rate: Disability rate is defined as the number of calendar days lost per employee per unit of time (month or year). The formula is as follows:

$$\frac{\text{No. of calendar days of absence due to nonoccupational illness (or injury) per month or year}}{\text{Av. no. of employees on payroll}}$$

$$\text{Disability Rate} = \frac{\text{Frequency Rate} \times \text{Severity Rate}}{1{,}000}$$

Note: Another method to compute frequency and severity rates for occupational injuries is that recommended by the National Safety Council. The Frequency Rate is the number of disabling work injuries per million employee-hours of exposure. The Severity Rate is the total days charged for work injuries per million employee-hours of exposure.

Diagnosis and Diagnosis Groupings.—It is recognized that one of the basic problems in collecting information will be the classification of illness and injury. The American Medical Association has played an important role over the past 25 years in developing and revising "The Standard Nomenclature of Diseases and Operations," and in recommending that it be used as the basic reference source for proper terminology of clinical diagnoses. The Standard Nomenclature is a classification of accepted terminology in use by the majority of hospitals in the United States for diseases and operation index filing. It is presently undergoing a major revision so that it can be used as a clinical-statistical classification when completed. The Committee is therefore not recommending the establishment of, or adherence to, any specific groupings at this time but plans to recommend the use of Standard Nomenclature categories when the revision is completed and made available to all physicians.

Records.—An infinite variety of forms could be devised and made to serve to record the essential information. These range from spread-sheet to punch card systems. Since another committee of the American Medical Association has the responsibility for developing suggested record-keeping forms, the Committee on Medical Care for Industrial Workers is merely noting at this time the various types of data which should be called for in such forms. Physicians and others responsible for the compilation and analysis of morbidity data are invited to submit the results of their analyses, together with copies of forms developed, to the Committee for possible future publication.

The items in the table are among those suggested for inclusion in sick absence records in individual and/or consolidated (group) records and reports. They do not preclude the addition of other items considered necessary by individual physicians or companies for other types of analyses.

Some Items Suggested for Inclusion in Sick Absence Records

- Name or identifying number
- Sex
- Marital status
- Department
- Occupation (see text, Appendix A, for definitions
  - Salaried
    - Managerial and supervisory
    - Clerical and sales
  - Production (hourly)
    - Semi-skilled and unskilled
    - Skilled
- Length of service with company (yr.)
  - Less than 1
  - 1- 4
  - 5- 9
  - 10-14
  - 15-19
  - 20-24
  - 25 and over
- Date of beginning of absence
- Date of return to work or other termination
- Duration of absence in calendar days
- Date of birth
- Age group (yr.)
  - Under 25
  - 25-34
  - 35-44
  - 45-54
  - 55-64
  - 65 and over
- Diagnosis
  - (Standard Nomenclature, 5th Edition—in preparation)
- Classification
  - Nonoccupational illness
  - Nonoccupational injury
  - Occupational illness
  - Occupational injury
- Number of days of paid sick leave allowed
- Calendar days of absence (days)
  - 1
  - 2
  - 3
  - 4- 7
  - 8- 14
  - 15- 28
  - 29- 49
  - 50- 91
  - 92-182
  - 183 and over
- Reason for termination
  - Returned to work
  - Discharged
  - Resigned
  - Retired
  - Deceased

Some Rules to Be Observed.—(*a*) The same person may be involved in more than one absence in the course of a month or a year. Therefore, it is important to record not only the total number of absences but also the actual number of people involved. (*b*) Where more than one diagnosis is involved in an absence, the absence and all calendar days lost should be attributed to the diagnosis associated with the condition causing the greatest loss

of days. (*c*) Each absence caused by an acute illness or an acute episode in the course of a chronic illness is to be considered as a separate absence. However, a person who returns to work before he has fully recovered from an acute illness or an acute episode in the course of a chronic illness and who consequently has to be absent again, should be considered as having had one continuous absence instead of two absences. The determination as to whether recovery from an acute illness, or an acute episode in the course of a chronic illness is incomplete, is one to be made according to individual company practice and medical judgment. (*d*) To facilitate record keeping and to avoid counting as two or more absences an absence which begins in one reporting period and continues into and through a subsequent reporting period(s), the arbitrary rule will be that such an absence will be charged against the reporting period in which it ends. Many organizations may find it difficult or undesirable to adhere to this rule, especially if they have been accustomed to computing absence data at the end of each calendar year. The reports of companies which wish to continue this practice should clearly indicate this fact, so that the basis for data compiled will be understood. (*e*) Where, upon operation of the rule stated in the first sentence of *d*., prolonged absence(s) would tend to exaggerate unduly the rate for any reporting period, the circumstances should be explained in a footnote.

Records containing the foregoing items and condition of recording information will be able to provide uniform data for the (1) three basic measures of absence, and, (2) various relationships involving age, occupation, sex, length of employment, and other factors considered of interest and importance.

Appendix A

Definitions of Occupations. Definitions of occupations (see table) are as follows:

Managerial and Supervisory: Managerial and supervisory classification includes officers of company, department managers, supervisors, and foremen. This category also includes technical and professional staff personnel such as accountants, auditors, editors, engineers, lawyers, physicians, nurses, and statisticians. These occupations include all those responsible for policy-making, planning, advising, coordinating, or guiding the work of others.

Clerical and Sales: Clerical and sales classification includes all nonsupervisory office personnel and those performing clerical duties such as shipping and receiving clerks, and stock clerks. This category also includes sales personnel such as canvassers, solicitors, demonstrators, and shoppers.

Skilled: Skilled classification includes craft and manual operations requiring a thorough and comprehensive knowledge of the processes involved in the work, the exercise of considerable independent judgment, a high degree of manual dexterity and, often, responsibility for valuable equipment and product. This group of workers becomes qualified by serving apprenticeships or extensive training periods.

Semi-skilled and Unskilled: Semi-skilled and unskilled classification includes all other production or hourly paid workers or service personnel not included in the previous classifications.

MEDICAL SCHOOL AND PRACTICE LIAISON

The A. M. A. Board of Trustees has endorsed the creation of a four-way liaison committee to bring about closer relationships between medical education and the practice of medicine. The group will be comprised of two members of the Board of Trustees, two presidents of universities having medical schools, two representatives of the Council on Medical Education and Hospitals, two designates of the Association of American Medical Colleges, and respective staff members.

Names of committee members were not immediately announced, pending final decision on selection by all groups concerned. Unlike the special committee formed early this year to mediate differences between some medical educators and some medical practitioners in Georgia (see editorial, "Concord Out of Conflict," THE JOURNAL, Aug. 30, 1958, page 2206) the new committee is not designed to help solve an existing local problem but, rather, to function on a long-range basis—building rapport and nipping incipient problems before they arise.

NEW EDITION OF AMERICAN MEDICAL DIRECTORY AVAILABLE

The new 20th edition of the American Medical Directory, which gives brief professional data about 250,621 physicians in the United States and Canada, is now available. The directory lists for each physician his age, address, date of licensure, specialty, and membership in special medical societies.

This edition contains 18,398 new names of physicians that did not appear in the last previous edition (1956) of the directory and also the names of 1,214 physicians whose addresses are unknown. The states with the biggest gains include California, 1,467; Florida, 476; Michigan, 395; Ohio, 324; Washington, 136; Oregon, 84; Arizona, 70. Among those in the loss column are Minnesota, 50; Iowa, 33; Missouri, 31.

Single copies of the directory sent anywhere in the United States or its possessions cost $35, and to other countries the cost is $38. Orders may be sent to these headquarters.

JOINT CONFERENCE COMMITTEES

Noting that joint and separate responsibilities which doctors and hospitals have in providing medical care and hospital services "cannot be discharged effectively without proper liaison," The A. M. A. Board of Trustees and the American Hospital Association's Board of Trustees have endorsed a recommendation that every hospital set up a Joint Conference Committee made up of representatives from its medical staff and its administrative staff. The recommendation first was made last February in a statement by the A. M. A. Council on Medical Education and Hospitals. Such committees are necessary, according to a preamble of the statement, because "they will bring to bear on major decisions which must be made in the hospital a full measure of broad experience, intelligence and responsibility. . . . There should be a common ground where these two groups can meet in order that there may be a mutual understanding of each other's activities and problems as the art and science of medicine become more complex and more comprehensive."

World Medical Association at Copenhagen

Scenes from 12th Assembly, Aug. 15-29, 1958

A, W.M.A. officials applaud address of welcome to Copenhagen. *Left to right* are Secretary General Louis H. Bauer, retiring President Ahmet Rasin Onat of Turkey, Council Chairman L. G. Tornal of Spain, and W.M.A. Journal Associate Editor S. S. B. Gilder of Canada. *B*, A. Lawrence Abel *(left)*, who presented medical film on "Hemorrhoids and the Early Detection of Rectal Cancer," is congratulated by Denmark's Prime Minister Hans Christian Hansen. Dr. John Henderson *(center)*, Medical Director of Johnson & Johnson, delivered keynote address. *C*, Dr. Louis H. Bauer *(left)*, Secretary General of the W.M.A., and Dr. Gunnar Gundersen *(second from left)*, President of the A.M.A., congratulate Dr. Charles Jacobsen *(far right)* on his election as President of W.M.A. Looking on is Hans Christian Hansen. *D*, Dr. Malcolm R. Hill, of Los Angeles, presents his film, "Anorectal and Sigmoidoscopic Examination with Differential Diagnosis." *E*, *Left to right* are A.M.A. President-elect Louis M. Orr, who delivered scientific paper on "The Biological Effects of Nuclear Radiation"; A.M.A. President Gunnar Gundersen; and A.M.A. Executive Vice-president F. J. L. Blasingame. *F*, Two Japanese physicians congratulate A.M.A.'s Mr. Ralph P. Creer on International Medical Film Exhibit. At *left* is Dr. Tomio Ogata of Tokyo, Vice-president of the General Assembly of Japanese Medical Congress. At *center* is Hiroshi Ishii of Tokyo, Supervisor of the Japanese Medical Association.

COMMITTEE ON INFLUENZA

In the fall of 1957 the A. M. A. Special Committee on Influenza cooperated with state medical societies, the U. S. Public Health Service, and other medical and health groups in the initiation and operation of mass immunization programs designed to combat the spread of Asian influenza. While there is no present threat of another Asian influenza epidemic, there is a continuing necessity for the immunization of certain groups and individuals. Therefore, the Committee believes that the following recent announcement by the U. S. Public Health Service is of interest to all physicians.

FRANK W. BARTON, *Secretary.*

INFLUENZA VACCINATION

The Public Health Service has recommended consideration of influenza vaccination among groups wishing to guard against absenteeism in their professions or occupations, and among those to whom the disease might be an added health risk. The Service pointed out that there are now ample supplies of influenza vaccine of the polyvalent type, containing immunizing material against the important strains of influenza, including the Asian strain, and that vaccination should be planned before the fall season begins. Dr. Leroy E. Burney, surgeon general of the Public Health Service, said that while there is no indication at present that widespread attacks of influenza will occur this fall and winter there undoubtedly will be some influenza and that vaccination is a prudent measure for certain groups and individuals.

Dr. Burney stressed that practicing physicians should be the judges of whether or not to vaccinate individuals. He said groups which should be considered for vaccination include hospital staffs whose services are necessary to the care of the sick; groups living in close proximity where influenza could spread rapidly, such as institutions; industrial or service groups, big or small, in occupations where the sudden absence of a sizable part of the force would create serious disruption of the work; and individual patients or groups who have a special risk, such as the aged, the chronically ill, and pregnant women. This special risk group, Dr. Burney said, should be the special area of consideration for the private physician.

COUNCIL ON MEDICAL SERVICE

UNION HEALTH CENTERS, 1958 SURVEY

The Committee on Medical Care for Industrial Workers of the Council on Medical Service and the Council on Industrial Health has recently completed a third survey of union health centers. A forthcoming publication will contain descriptions of 29 such centers together with data on various aspects of their operations. (A previous announcement in THE JOURNAL gave the figure as 28. An additional plan has since been surveyed.) The 29 centers represent more than half of the 50 union health centers in operation which have an enrollment of approximately 950,000 union members and, in some instances, dependents.

Union health centers have emerged as a major development in the provision of medical care to members of unions only within the past 15 years. The earliest center was that of the International Ladies' Garment Workers' Union in New York City, which was organized in 1913. It was not until World War II, when the government's anti-inflation "hold-the-line" order virtually halted wage increases, that health and welfare plans became matters of prime importance in labor-management negotiations and collective bargaining. Medical services provided through these health centers range from diagnostic only to comprehensive medi-

Members of the Committee on Medical Care for Industrial Workers are Drs. Frank J. Holroyd, Chairman, Princeton, W. Va.; T. J. Danaher, Torrington, Conn.; Edwin P. Jordan, Charlottesville, Va.; Melvin N. Newquist, New York; Leo Price, New York; William A. Sawyer, Rochester, N. Y.; Frederick W. Slobe, Chicago; Clyde C. Sparks, Ashland, Ky.; Donald A. Dukelow, Consultant; Mr. Edwin J. Holman, Consultant; Dr. B. Dixon Holland, Secretary, Council on Industrial Health; Mr. George W. Cooley, Secretary, Council on Medical Service; and Mr. Murray Klutch, Research Associate, Chicago.

cal care, although "comprehensive" features vary according to the specific plan. Most health centers, however, provide diagnostic and ambulatory medical care through closed panels. Physicians are, for the most part, employed on an hourly or session basis, although a small number receive a salary or retainer for their services. In a few instances, physicians in private group practice contract to render the specific services negotiated through the contract between the union and the employer.

Table 1 is a listing of the 29 union health centers surveyed showing their dates of origin, eligible and actual membership, whether dependents and retired members are covered, the number of union locals involved in each program, and the scope of the medical program offered.

As previously indicated, the ILGWU Union Health Center in New York City is the oldest one in existence, having been organized in 1913. This union, incidentally, has the largest number of health centers throughout the United States. Of the remaining 28, 6 were begun prior to 1950, and the majority since then. The enrollment in 28 of the plans for which such information was available was over 765,000. This represents 80% of the estimated enrollment in all union health centers as of

TABLE 1.—*Date of Origin, Membership, and Scope of Medical Programs of Twenty-nine Union Health Centers, 1958 Survey, Committee on Medical Care for Industrial Workers**

Plan	Date Begun	Total Eligible	Total Members	Dependents Covered	No. of Locals Concerned	No. of Firms Concerned	Scope of Program
Amalgamated Clothing Workers of America†							
Chicago	1955	10,000	9,500	Spouses, retired members	N.A.§	Over 100	Diagnostic, ambulatory medical care
New York and New Jersey (Mobile Unit)	1957	3,000	3,000	None	1	57	Diagnostic only
New York	1951	33,356	33,356	Spouses	26	N.A.	Diagnostic, ambulatory medical care
Philadelphia	1951	23,000	23,000	Spouses	N.A.	Several hundred (tabulated as 300)	Diagnostic, ambulatory medical care
International Ladies' Garment Workers' Union							
Allentown, Pa.	1948	12,000‡	12,000	None	5	220	Diagnostic only
Boston	1949	15,000	15,000	None	52	N.A.	Diagnostic, ambulatory medical care
Chicago	1955	7,000	7,000	None	10	250	Diagnostic, ambulatory medical care
Cleveland	1952	5,000	5,000	None	13	N.A.	Diagnostic only
Harrisburg, Pa. (Mobile Unit)	1951	N.A.	N.A.	None	N.A.	75	Diagnostic only
Kansas City, Mo.	1950	2,502	2,502	None	9	40	Diagnostic, ambulatory medical care
Los Angeles	1951	9,441	9,441	None	14	220	Diagnostic, ambulatory medical care
Minneapolis	1950	800‡	800	None	5	18	Diagnostic, ambulatory medical care
Newark, N. J.	1951	30,000	30,000	None	34	617	Diagnostic only
New York	1913	155,000	155,000	Spouses, retired members, children under 18	32	N.A.	Diagnostic, ambulatory medical care
Philadelphia	1944	21,071	21,071	None	N.A.	N.A.	Diagnostic, ambulatory medical care
Springfield, Mass. (Mobile Unit)	1947	2,400	2,400	None	N.A.	17	Diagnostic only
Wilkes-Barre, Pa.	1948	21,566	21,566	None	5	256	Diagnostic only
Amalgamated Laundry Workers, New York	1954	18,000	18,000	Spouses and retired members, children for special programs	13	1,400	Diagnostic, ambulatory medical care
Amalgamated Lithographers of America, New York	1953	7,500	7,500	None	1	300	Diagnostic, ambulatory eye care
American Federation of Labor Medical Service Plan, Philadelphia	1951	52,000	32,000	Families of members	28	300	Diagnostic, ambulatory medical care
Building Service Employees (Local 32B) International Union, New York	1957	36,000	36,000	None	1	N.A.	Diagnostic, ambulatory medical care
Medical Department: Pension Committee of the Joint Industry Board of the Electrical Industry, New York	1953	7,000	7,000	None	1	N.A.	Diagnostic only
New York Hotel Trades Council and Hotel Association of New York City	1956	34,000	34,000	None (Retired members)	20	279	Diagnostic, ambulatory and in-hospital medical care
New York Shipping Association—International Longshoremen's Association (Ind.), Brooklyn	1957	40,000	12,000	None	N.A.	N.A.	Diagnostic only
Union Eye Care Center, Chicago	1951	92,734	92,734	Families	106	N.A.	Diagnostic, ambulatory eye care
Union Health Service, Inc., Chicago	1955	10,424	10,424	(about 5%)	7	400	Comprehensive medical care
United Wire, Metal and Machine Medical Center, New York	1955	10,000	4,000	Spouses and children under 18	2	200	Diagnostic, ambulatory medical care
Warehouse and Distribution Workers Union, Local 688, Labor Health Institute, St. Louis	1945	15,849	6,361	Families	1	200	Comprehensive medical care
Willys Unit, Local 12, UAW, Toledo	1955	155,463	155,463	Spouses and children	103	N.A.	Diagnostic only
Totals		830,196 (28 plans)	766,178 (28 plans)		489 (23 plans)	5,259 (19 plans)	10 Diagnostic only 17 Diagnostic, ambulatory medical care 2 Comprehensive

* Data as of Dec. 31, 1957, unless otherwise indicated. Plans arranged, for most part, according to union sponsorship; exact names of union health centers will be found in section of forthcoming publication describing each plan.

† Health centers are named Sidney Hillman.

‡ 1952.

§ N.A. = not available.

the end of 1957. Eleven plans, with an enrollment of approximately 530,000, included one or more dependents. Three of the 11 which covered dependents also included retired members; one other plan which did not include dependents also covered retired members. Of the 29 health center programs, 23 for which information was available were participated in by 489 local unions. In most cases, these locals are part of the union. In a few instances, such as the American Federation of Labor Medical Service Plan, the St. Louis Labor Health Institute and Willys Unit, Local 12, other unions may also affiliate with the plan. These are generally called multiunion programs. One of the characteristics of these union health centers is that their members usually, but not always, work in relatively small establishments or units which are widely separated and have little or no in-plant medical services by occupational health program. Over 5,200 firms were involved in the collectively bargained agreements supporting these centers of the 19 programs for which such information was made available. As previously indicated, most health centers provide diagnostic and ambulatory medical care. Of the 29 union health centers surveyed, 17 offer these medical services, 10 provide diagnostic programs only, and 2 offer a more or less comprehensive program.

Table 2 is a breakdown of the personnel employed by the union health centers surveyed. Over 1,100 physicians are employed on a part-time basis (hourly or per session), and generally work at the center two or three days a week for periods of two

TABLE 2.—*Personnel and Payment to Physicians in Twenty-nine Union Health Centers, 1958 Survey, Committee on Medical Care for Industrial Workers*

Plan	Administrative	Physicians	Nurses	Ancillary	Payment to Physicians (Exclusive of Medical Director)*
Amalgamated Clothing Workers of America					
Chicago	9	30	4	10	$9 per hr., 1st yr.; $9.50 per hr., 2d yr.; $10 per hr., 3d yr.
New York and New Jersey (Mobile Unit)	4	3	1	4	Retainer
New York	22	77	7	15	$5.75 for general practitioners; $7.75 for specialists
Philadelphia	37	44	5	14	$7.00 per hr., 1st yr.; $8.50, 2d yr.; $10, thereafter
International Ladies' Garment Workers' Union					
Allentown, Pa.	6	24	2	2	$7 per hr.
Boston	6	35	3	4	$7 per hr.
Chicago	2	26	4	6	$8.50 per hr.
Cleveland	3	34	1	2	$30 per 2-hr. session
Harrisburg, Pa. (Mobile Unit)	2	31	4	4	$15 per 2½-hr. session
Kansas City, Mo.	1	31	4	3	$10 per hr., 1st 5 years; $11 thereafter
Los Angeles	9	39	5	6	$12 per hr.
Minneapolis	37	44	5	13	$7 per hr., 1st yr.; $8.50 per hr. 2d yr.; $10, thereafter
Newark, N. J.	2	23	5	9	$15 per 2-hr. session
New York	142	175	42	40	Salary and hourly†
Philadelphia	16	32	4	9	$7 per hr., 1st yr.; $8 per hr., 2d yr.
Springfield, Mass. (Mobile Unit)	...	1	...	1	Not stated
Wilkes-Barre, Pa.	1	35	4	4	$8 per hr.
Amalgamated Laundry Workers, New York	17	45	3	9	$7.75 per hr.
Amalgamated Lithographers of America, New York	1	7	1	3	$9—9.50 for ophthalmologists; $8.25 for others
American Federation of Labor Medical Service Plan, Philadelphia	N.S.†	62	10	7	$7 per hr.
Building Service Employees (Local 32B) International Union, New York	9	27	3	4	$8 per hr.
Medical Department: Pension Committee of the Joint Industry Board of the Electrical Industry, New York	4	N.S.	1	5	Not stated
New York Hotel Trades Council and Hotel Association of New York City	35	170	15	13	$7.50 per hr., general practitioners; $10 per hr., specialists
New York Shipping Association—International Longshoremen's Association (Ind.), Brooklyn	2	30	7	25	$9 per hr., generalists; $12 per hr., specialists
Union Eye Care Center, Chicago	6	6	...	5	$10 per hr.
Union Health Service, Inc., Chicago	11	22	4	5	Time proportion basis; based on annual salaries of $15,000-$20,000 per yr.
United Wire, Metal and Machine Medical Center, New York	1	19	2	1	$25 per 3-hr. session, general practitioners; $10 per hr., specialists
Warehouse and Distribution Workers Union, Local 688, Labor Health Institute, St. Louis	1	56	12	14	Hourly rate based on Dept. of Commerce income statistics for indicated specialties
Willys Unit, Local 12, UAW, Toledo	14	6	3	5	Salary
Totals	400 (28 plans)	1,140 (28 plans)	161	242	

* Virtually all medical directors are on salary for their part-time or full-time employment.
† N.S. = not stated.
‡ $5.50-$10 per hr. Greatest number receive $6.50 per hr. Salaries of chiefs of services range from $5,000 to $8,000 per yr.

or three hours. In some instances, these private practitioners work as many as 20 hours a week. Hourly rates for general practitioners range from $5.75 to $10 per hour; those for specialists range from $7 to $12 per hour. The 29 plans employ 161 nurses of various qualifications, and 242 auxiliary and ancillary personnel, including laboratory and x-ray technicians, social workers, and medical librarians.

plans it ranged from 31 to 50%; in 3 plans utilization ranged from 51 to 75%; and in one plan offering comprehensive medical care it was over 89%. It should be noted that these percentages are based on figures supplied by the plans. They may or may not be accurate inasmuch as there are no uniform criteria or definitions for recording various types of data among the administrators of these plans. The footnote of table 3 offers one explanation for

TABLE 3.—*Number of Persons in Plan and Number Utilizing Union Health Centers, 1958 Survey, Committee on Medical Care for Industrial Workers**

Plan	No. of Persons in Plan	No. Utilizing Services	% of Persons Utilizing Services Over 1-Yr. Period†
Amalgamated Clothing Workers of America			
Chicago	9,500	4,400 (Sept. 12, 1955, to March 1, 1956)	18.8
New York and New Jersey (Mobile Unit)	5,000	700 (5 mo. of 1957)	56.0
New York	33,356	30,000 (1951 to Dec. 31, 1957)	12.8
Philadelphia	23,000	7,500	32.6
International Ladies' Garment Workers' Union			
Allentown, Pa.	12,000	4,971 (April 1, 1951, to April 1, 1952)	41.4
Boston	15,000	3,176	21.2
Chicago	7,000	2,350	33.6
Cleveland	5,000	2,714 (Feb. 26, 1952, to Dec. 31, 1957)	7.6
Harrisburg, Pa. (Mobile Unit)	Not stated	9,691 (Oct., 1946, to Oct., 1951)	....
Kansas City, Mo.	2,502	1,304	50.9
Los Angeles	9,441	3,258	34.5
Minneapolis	800	552 (1952)	69.0
Newark, N. J.	30,000	10,407	34.7
New York	155,000	40,819	26.3
Philadelphia	21,071	6,000	28.8
Springfield, Mass. (Mobile Unit)	2,400	3,639 (Dec., 1947 to Dec., 1957)	15.1
Wilkes-Barre, Pa.	21,501	9,039	41.9
Amalgamated Laundry Workers, New York	18,000	3,721 (March 31, 1956, to March 31, 1957)	20.7
Amalgamated Lithographers of America, New York	7,500	2,600	34.7
American Federation of Labor Medical Service Plan, Philadelphia	32,000	13,600	42.5
Building Service Employees (Local 32B) International Union, New York	30,000	2,529 (Dec. 1, 1957, to April 30, 1958)	16.9
Medical Department: Pension Committee of the Joint Industry Board of the Electrical Industry, New York	7,000	6,300 (April, 1955, to July, 1955)	38.6
New York Hotel Trades Council and Hotel Association of New York City	34,000	12,150	35.7
New York Shipping Association—International Longshoremen's Association (Ind.), Brooklyn	12,000	3,382 (Sept. 24 to Dec. 31, 1957)	104.71
Union Eye Care Center, Chicago	92,734	5,060 (1956)	5.5
Union Health Service, Inc., Chicago	10,424	2,483	23.8
United Wire, Metal and Machine Medical Center, New York	4,000	2,345	58.6
Warehouse and Distribution Workers Union, Local 688, Labor Health Institute, St. Louis	6,361	11,354 (1955-1956)	89.2
Willys Unit, Local 12, UAW, Toledo	155,462	8,397 (July, 1955, to Jan. 1, 1958)	21.1

* Data as of December, 1957, unless otherwise indicated.
† Percentage utilization computed on yearly basis where utilization is indicated for more or less than a 1-yr. period.
‡ One explanation for this figure is that it possibly includes all visits made to the plan by a member. The requests data on utilization did not ask for patient-visits.

Table 3 is concerned with the number and percentage of persons utilizing the health centers' services over a one-year period. Where utilization figures were made available for more or less than a one-year period, the percentages were computed on an annualized basis. Yearly utilization ranged from a low of 5.5% in one plan to a high of 89.2% (excluding the plan with the footnote explanation and the plan with incomplete enrollment information). Of the 27 plans, 2 had a utilization of less than 10%; in 5 plans utilization ranged from 10 to 20%; in 5 plans it ranged from 21 to 30%; in 11 possible overstatement of utilization rates. There are other explanations which may similarly affect such rates.

Table 4 indicates the sources and methods of financing of the 29 union health centers surveyed. Collective bargaining represents the primary source of monies for which support of the centers is received. Varying arrangements exist among different unions for allocating portions of its health and welfare benefits for the operation of their health centers. Contributions from management constitute the only source of support for 25 such programs.

In one case, the union finances the entire cost of the program, presumably from members' dues. In one program, union members are assessed an amount above and beyond the employers contributions. In one program patients' fees for service rendered support the program, although the unions involved purchase shares to join the program and assume responsibility for any deficit incurred. Another program is maintained by a combination of employer contributions, union fees and contributions, and fees for service to members.

The tables and text presented here contain some of the highlights of the forthcoming publication by the Committee on Medical Care for Industrial Workers. The 1958 survey treats each union health center as a specific case study, and for each plan includes information and data on (1) history; (2) membership; (3) objectives of programs; (4) facilities; (5) financing; (6) budget and operating costs; (7) administration; (8) business and professional personnel; (9) benefits; and (10) preventive aspects of the services.

TABLE 4.—*Source and Methods of Financing of Twenty-nine Union Health Centers, 1958 Survey, Committee on Medical Care for Industrial Workers*

Plan	Source	Method of Financing
Amalgamated Clothing Workers of America		
Chicago	collective bargaining	Employer contributions to Social Benefit Fund; fund allocated $2.60 per mo. per member in 1956 and 1957
New York and New Jersey (Mobile Unit)	collective bargaining	Portion of employer contribution to Sick Benefit Fund (not stated)
New York	collective bargaining	Employers contribute 0.25% of gross payroll for operations of center; members assessed $10 annually
Philadelphia	collective bargaining	Employers contribute 0.75-1% of payroll; members assessed $20 to start program
International Ladies' Garment Workers' Union		
Allentown, Pa.	collective bargaining	Employer contributes 2% of gross payroll for health and welfare benefits, part of which maintains center
Boston	collective bargaining	Employer contributes 6.5% of gross payroll for health and welfare benefits, 2% of which maintains center
Chicago	collective bargaining	Employer contributes 1% of gross payroll to trust fund; fund allocates $1 per mo. per member to center, and makes up any deficit
Cleveland	collective bargaining	Employer contributes 3.5% of gross payroll to Health Fund, part of which maintains center
Harrisburg, Pa. (Mobile Unit)	collective bargaining	Amount contributed by employers not stated
Kansas City, Mo.	collective bargaining	Employers contribute 1% of gross payroll
Los Angeles	collective bargaining	Employers contribute percentage of gross payroll, portion of which maintains center
Minneapolis	collective bargaining	Employers contribute 1% of gross payroll
Newark, N. J.	collective bargaining	Employers contribute percentage of gross payroll, portion of which maintains center
New York	collective bargaining	Employers contribute 3.5-5% of gross payroll, portion of which maintains center
Philadelphia	collective bargaining	Employers contribute 6.9% of gross payroll; center receives 0.5%
Springfield, Mass. (Mobile Unit)	collective bargaining	Employers' contributions (amount not stated)
Wilkes-Barre, Pa.	collective bargaining	Employers contribute 3.5-5% of gross payroll, 2% of which is allocated to the center
Amalgamated Laundry Workers, New York	collective bargaining	Employers contribute 3% of payroll, portion of which maintains center
Amalgamated Lithographers of America, New York	collective bargaining	Employers contribute $4 per wk. per employee to Sickness and Accident Fund; less than 10% of this supports the center
American Federation of Labor Medical Service Plan, Philadelphia	collective bargaining	Employers' contributions to first fund according to individual contracts; local unions assessed $15 per single member, $30 for couple, and $37.50 for family (including children up to 9 years of age) for operation of center
Building Service Employees (Local 32B) International Union, New York	Union finances entire cost of program	
Medical Department: Pension Committee of the Joint Industry Board of the Electrical Industry, New York	collective bargaining	Employers contribute 5% of payroll to fund, a portion of which supports center
New York Hotel Trades Council and Hotel Association of New York City	collective bargaining	Employers contribute 5.5% of payroll to welfare program, a portion of which supports center
New York Shipping Association—International Longshoremen's Association (Ind.), Brooklyn	collective bargaining	Employers contribute 14 cents per hr. to welfare fund, of which 3 cents go toward operation of center
Union Eye Care Center, Chicago	Shares in $50 unit purchased by unions	Patients' fees and service assessment on unions support center
Union Health Service, Inc., Chicago	collective bargaining	Employers contribute to union welfare funds; unions pay plan $3 per mo. per member, $6 for a couple, and $7 for family
United Wire, Metal and Machine Medical Center, New York	collective bargaining	Employers contribute percentage of gross payroll to welfare fund, a portion of which operates center; originally supported by union
Warehouse and Distribution Workers Union, Local 688, Labor Health Institute, St. Louis	collective bargaining	Employers contribute 5% of payroll to welfare program, a portion of which supports center
Willys Unit, Local 12, UAW, Toledo	collective bargaining	Union contributions, members' fees—employer contributes 4 cents per hr. per employee; $25 affiliation fee paid by local unions; unions contribute 3 cents per member per mo.; patients pay reduced fees for certain services

MEDICAL NEWS

CALIFORNIA

Dr. Rigler Awarded Medal.—At the recent annual meeting of the American Roentgen Ray Society in Washington, D. C., Dr. Leo G. Rigler of Los Angeles was awarded the Caldwell medal. Dr. Rigler, visiting professor of radiology at University of California at Los Angeles School of Medicine and currently president of the Radiological Society of North America, presented the annual Caldwell lecture, which was established in honor of the late Dr. Eugene W. Caldwell, New York City, past-president of the American Roentgen Ray Society.

University News.—Dr. Edwin O. Field, Division of Radiobiology, Radiotherapy Department, Royal Marsden Hospital, London, has been appointed visiting instructor in medicine at Stanford University School of Medicine, San Francisco, for the academic year 1958-1959. Dr. Field will collaborate on hemotology research being conducted in the isotope laboratory by the departments of medicine and radiology.

COLORADO

University News.—Two research grants to members of the University of Colorado School of Medicine faculty for studies in muscular dystrophy and heart surgery have been announced. The Muscular Dystrophy Association of America, Inc., of New York City, has renewed for another year a grant of $21,500 for research by Cosmo G. Mackenzie, Sc.D., head, department of biochemistry. The project is titled "Identity and Treatment of the Primary Biochemical Lesions in the Muscular Dystrophies." A grant of $15,565 has been made to Dr. Ben Eiseman, professor of surgery, for a study of "Cardiac Valve Substitutes," by the National Heart Institute, Bethesda, Md.——A grant of $24,626, "to enhance the teaching program" of the department of physical medicine and rehabilitation, University of Colorado School of Medicine, Denver, has been received from the Office of Vocational Rehabilitation, U. S. Department of Health, Education and Welfare.

DISTRICT OF COLUMBIA

Society News.—The Washington, D. C. Dermatological Society has elected the following officers for 1958-1959: chairman, Dr. Raymond A. Osbourn, vice-chairman, Dr. Peter N. Horvath, and secretary-treasurer, Dr. June C. Shafer, (Arlington, Va.). Meetings will be held in Washington, D. C., on the fourth Thursday of every month, September through May.

Personal.—Dr. Mathew Ross, formerly of Beverly Hills, Calif., has taken office as medical director of the American Psychiatric Association in Washington, D. C., succeeding Dr. Daniel Blain, who resigned Sept. 1.——Dr. Benjamin Karpman, chief psychotherapist and consultant at Saint Elizabeths Hospital, was invited by the British Institute for the Study and Treatment of Delinquency to lecture in England on general psychiatric problems, Aug. 18-22. Dr. Karpman later spoke before the Spanish Psychological Society.

ILLINOIS

General Practitioners Meet in Chicago.—The 11th annual meeting of the Illinois Academy of General Practice will be at the Morrison Hotel, Chicago, November 3-6. There will be seven sessions of the scientific assembly, including, among other presentations, a panel of experts to answer questions on the business side of medicine; an academy film, "Building for Tomorrow"; the annual dinner dance Wednesday evening; and exhibits. The president and president-elect are, respectively, Drs. Abraham I. Doktorsky and Robert E. Heerens.

Society News.—The following officers of the Illinois Psychiatric Society have been elected for 1958-1959: president, Dr. Nathaniel S. Apter, Chicago; president-elect, Dr. Frances Hannett, Chicago; secretary-treasurer, Dr. Paul E. Nielson, Chicago; and councilors, Drs. Kalman Gyarfas, Chicago, and Lester H. Rudy, Galesburg.——The Illinois Society of Anesthesiologists has elected the following officers: president, Dr. Huberta M. Livingstone, Chicago; vice-president, Dr. Lawrence D. Ruttle, Joliet; secretary, Dr. Clifford A. Baldwin Jr., Wilmette; and treasurer, Dr. Robert F. Finegan, Elgin.

MASSACHUSETTS

Dr. Martha Eliot Awarded Medal.—At the 86th annual meeting of the American Public Health Association, October 28, in St. Louis, the Sedgwick Memorial Medal was presented to Dr. Martha May Eliot, head, department of maternal and child health, Harvard University School of Public Health, Boston, for "distinguished service in public health." Dr. Eliot formerly chief, U. S. Children's Bureau,

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Washington, D. C., in 1947 was the first woman to be elected president of the American Public Health Association. She is a distant relative of the late Charles W. Eliot, president of Harvard University.

University News.—Boston University has received $50,000 from the American Cancer Society, Massachusetts Division. It will be added to funds now being raised for the construction of a 3-million-dollar medical research building. The university has received $900,000 in a $1,500,000 drive to match a federal grant of a similar amount for this project.

MICHIGAN

Appoint Professor of Public Health.—The newly organized research and training service of the University of Michigan School of Public Health, Ann Arbor, will be under the direction of Dr. Hugh B. Robins, formerly health director of Calhoun County, who was appointed professor of public health practice, effective October 1. The research will be financed by a five-year grant of $167,620 from the W. K. Kellogg Foundation, Battle Creek. Dr. Robins, who has been a non-resident lecturer in the School of Public Health, formerly was health commissioner of Charleston, West Virginia.

Society News.—The new officers for 1958-1959 of the Western Michigan Pediatric Society are: president, Dr. John C. Montgomery, Grand Rapids; president-elect, Dr. Clarence L. Hoogerland, Alma; secretary-treasurer, Dr. Samuel S. Jacob, III, 201 Ann St., East Lansing; and assistant-secretary, Dr. Jerome E. Webber, Grand Rapids.

MISSISSIPPI

Society News.—The Mississippi Society of Anesthesiologists has elected the following officers: president, Dr. Thomas J. Marland, Jackson; vice-president, Dr. William E. Sheffield, Charleston; and secretary-treasurer, Dr. Curtis W. Caine, Jackson.

Personal.—Dr. Durward L. Blakey became director of the Division of Preventable Disease Control of the Mississippi State Board of Health on July 1, succeeding Dr. A. L. Gray, who was elevated to the position of state health officer.

University News.—Construction of 80 student housing units on the University of Mississippi School of Medicine campus has begun. Four buildings of 20 units each on Jackson's Lakeland Drive will furnish 44 two-bedroom and 36 efficiency apartments available to single or married students, interns, and residents. Cost of the project will be amortized from rent revenues.—The Mississippi Heart Association has awarded eight seeding research grants and a cardiovascular fellowship to The University of Mississippi School of Medicine, Jackson, totaling $18,800. The health agency also allocated $17,000 toward establishment of a cardiovascular chair at the new medical school.

MISSOURI

Research Training Grant in Microbiology.—The National Institute for Allergy and Infectious Diseases of the U. S. Public Health Service has made a grant of $225,690 for research training in microbiology and virology to St. Louis University School of Medicine, St. Louis, for a five year period. The new program will offer scientists who have Ph.D. degrees in other sciences an opportunity to broaden their training and experience along lines pursued in the microbiology department at this school of medicine. Opportunity will be offered also to provide research training in infectious diseases to young physicians who plan to make microbiology and related basic sciences their career. The new grant, which will augment research in microbiology for medical students, will be under the direction of Dr. R. Walter Schlesinger, director of the department, and Edwin L. Minard, Ph.D., associate professor of microbiology.

NEW JERSEY

Regional Meeting of College of Physicians.—The 13th regional meeting of the American College of Physicians (New Jersey) will be in the auditorium of the Mutual Benefit Life Insurance Company, 520 Broad St., Newark, N. J., November 12, to which all interested physicians and their wives are invited. The scientific program, limited to diseases of the adrenal gland, will be presented by members of the faculty of Columbia University College of Physicians and Surgeons, New York City. Following the symposium, Dr. Frank B. Berry, assistant secretary of defense (health and medical), Washington, D. C., will speak on the relationships between military and civilian medicine. The speaker at the informal dinner will be Dr. Dwight L. Wilbur, San Francisco, president of the American College of Physicians.

International Symposium on Tuberculosis.—Deborah Sanatorium and Hospital at Browns Mills, will sponsor an international symposium on tuberculosis, November 20-22. The morning and afternoon panel sessions will be held at the Bellevue-Stratford Hotel in Philadelphia. The general subjects of the six panels will be "Chemotherapeutic Prophylactic Measures for Tuberculosis"; "The Hospital and Home, Roles in Tuberculosis Management"; "The Problem of Relapse of Tuberculosis Lesions Under Chemotherapy"; "Duration of Drug Treatment"; "Pathological Problems"; "Tuberculosis Case-Finding"; "Surgical Aspects of Treatment of Tuberculosis"; and "The Future Problem of Tuberculosis, Program for its Control." Nearly 50 authorities in

this field will serve on the panels. Among the panel members from foreign countries will be Drs. Georges J. Canetti, Paris, France; Johannes Holm, Geneva, Switzerland; John R. Bignall, London, England; Hugh E. Burke, Montreal, Canada; Frederick R. Edwards, Liverpool, England; John M. Robson, London, England; Philip M. D'Arcy Hart, London, England; Frederick G. Kergin, Toronto, Canada; Carl B. Semb, Oslo, Norway, and Hans J. N. Ustvedt, Oslo, Norway. Registration is open without fee to all interested physicians and surgeons. This symposium, which has been endorsed by the National Tuberculosis Association, the American Trudeau Society, and the American College of Chest Physicians, is the first of a projected series under Deborah sponsorship.

Society News.—Officers of the Radiological Society of New Jersey for 1958-1959 are: Dr. George G. Green, Asbury Park, president; Dr. William L. Palazzo, Teaneck, vice-president; Dr. Andrew P. Dedick Jr., Red Bank, secretary; and Dr. William L. Bonnet, Trenton, treasurer. The meeting dates remain: annual meeting in May in Atlantic City; and the fall meeting, October-November, in Newark.

NEW YORK

Dr. Weiss Receives Lectureship Award.—The Albany Medical College of Union University has given its second annual honorary lectureship award to Dr. Paul A. Weiss of the Rockefeller Institute for Medical Research, New York City. This award is given in recognition of "distinguished service to mankind in the fields of science, medicine and teaching." Last year the award was given to William M. Clark, Ph.D., emeritus professor of physiological chemistry at Johns Hopkins University School of Medicine, Baltimore.

University News.—Dr. Ponduri Venketa Ramanarao, professor of bacteriology, Osmania Medical College, Hyderabad, capital of the state of Andhrapradesh, India, has joined the department of microbiology of the State University of New York Upstate Medical Center in Syracuse as a participant under an International Cooperation Administration training program.

Society News.—At the meeting of the New York Allergy Society, November 17, at the Beekman Tower Hotel, 1st Ave. and 49th St., New York City, 8:30 p. m., there will be a panel discussion on "The Single Repository Injection Treatment of Hay Fever," moderated by Dr. Robert A. Cooke, chief of the Institute of Allergy, Roosevelt Hospital, New York. Members of the panel will be Drs. Mary E. H. Loveless of Cornell University Medical College; John H. Mitchell and William F. Mitchell, both of Ohio State University Medical College; and William B. Sherman, chief of allergy, Presbyterian Hospital, New York.

New York City

Grant to Aid Liberian Institute.—The American Foundation for Tropical Medicine, 345 Madison Avenue, announces that Eli Lilly and Company of Indianapolis has made a grant to support the activities of the Liberian Institute of the foundation during the present year—an award similar to the one made by the same company last year. This support, the foundation says, has assisted in making possible expanded research activities of the institute in Liberia, West Africa.

Hospital News.—The Department of Pathology of The Mount Sinai Hospital, New York, has been awarded $171,000 by the U. S. Public Health Service as a research training grant for experimental pathology for five years. Under the program, training of residents and research fellows (trainees) in experimental pathology will be integrated with that of anatomical and clinical pathology. The grant also permits the appointment of a coordinator for the organization of the training in various techniques of experimental pathology.

Hungarian Association Meeting.—The annual Semmelweis meeting of the American Hungarian Medical Association will be November 14 at 8:30 p. m., at the New York Academy of Medicine, Hosack Hall. Dr. Max Thorek of Chicago, founder of the International College of Surgeons, will speak on "Impending Death Under Anesthesia," and Dr. Paul H. Hoch, New York State commissioner of mental hygiene, on "Some Remarks on Semmelweis from a Psychiatric Point of View." Dr. Alexander Borota is president of the society and Dr. G. Peter Halberg, secretary.

Annual Wyckoff Lecture.—Dr. Rodney Smith, senior surgeon to the Victoria Hospital for Children, London, England, and surgical tutor for the Royal College of Surgeons, will deliver the annual John Wyckoff lecture of the New York University College of Medicine at 4:30 p. m., November 5, in the Alumni Hall, 31st Street and First Avenue, on "Surgery Before and After John Hunter." The Wyckoff lecture is sponsored by the Phi Delta Epsilon Fraternity in honor of the late Dr. John H. Wyckoff, who was dean of the New York University College of Medicine from 1932 to 1937.

Conference on Study of Sex.—The first annual conference of the Society for Scientific Study of Sex will be at the Barbizon-Plaza Hotel on Nov. 8 at 9 a. m. The general subjects for discussion will be "Therapeutic Abortion" and "Frigidity." This new

society proposes to organize symposiums, seminars, workshops, and conferences to consider problems in the sexual area and later to publish a scientific journal devoted to relevant original studies and reports. The list of charter members contain names of medical scientists who are widely known for their research work. The chairman of the program committee is Dr. Hans M. Lehfeldt, 784 Park Ave., New York 21.

NORTH CAROLINA

New Chairman of Department of Microbiology.—Duke University School of Medicine, Durham, announces that Norman H. Conant, Ph.D., professor of mycology at Duke, has been appointed chairman of the department of microbiology to succeed Dr. David T. Smith, who has been head of the microbiology department since the school of medicine opened in 1930. Dr. Smith resigned as chairman in order to devote more time to teaching and research. He will retain his full professorship and continue as an active teacher. Dr. Conant joined the Duke medical faculty in 1935. He has held consulting and advisory posts that include tropical medicine consultant to the Secretary of War and member of the advisory panel for the office of naval research.

NORTH DAKOTA

General Practitioners Meeting at University.—Dr. Alan K. Johnson, Williston, N. D., president, North Dakota Chapter, American Academy of General Practice, announces that the annual meeting and postgraduate refresher course of the North Dakota Academy of General Practice will be held at the University of North Dakota School of Medicine, November 21-22. Members of the American Academy of General Practice from North and South Dakota and Minnesota are especially invited to attend, plus prospective members from any of these areas. Dr. Richard L. Varco, of the department of surgery, University of Minnesota, and Dr. Maurice H. Stauffer of the department of gastroenterology of the Mayo Clinic, will be guest speakers for the session. For information write Dr. Richard D. Nierling, % Jamestown Clinic, Jamestown, North Dakota.

OHIO

Phi Delta Epsilon Lectureship.—The annual lecture of Phi Delta Epsilon Fraternity, under the auspices of Beta Epsilon Chapter, will be held at the University of Cincinnati College of Medicine, November 20 at 8:30 p. m. The lecturer will be Dr. Claude S. Beck of Cleveland, who will speak on coronary heart disease.

Personal.—Dr. Relja Nedeljkovic has been appointed the Mannheimer Memorial Fellow at the May Institute for Medical Research of the Cincinnati Jewish Hospital. A native of Yugoslavia, Dr. Nedeljkovic spent five years in Belgium, where he engaged in research. At the May Institute, he is collaborating in studies on arteriosclerosis.

Dr. Page Receives Award.—The American Heart Association, at its annual meeting in San Francisco, October 25, gave its award for cardiovascular research to Dr. Irvine H. Page, director of research of the Cleveland Clinic Foundation. Dr. Page was cited for his contribution on hypertension. He will receive $2,500 and a scroll.

Dr. Levine to Lecture on Diabetes.—The Phi Delta Epsilon Fraternity, Upsilon Chapter, will hold its 1958 national lecture at the Cleveland Medical Library Auditorium, November 19, 8:30 p. m. The speaker will be Dr. Rachmiel Levine, chairman, department of medicine, Michael Reese Hospital, Chicago, and his subject will be "Problems in Etiology of Diabetes Mellitus."

OKLAHOMA

Society News.—The Oklahoma Society of Anesthesiologists has elected the following officers: president, Dr. Carl H. Guild, Jr., Tulsa; president-elect, Dr. Harlan K. Sowell, Oklahoma City; and secretary-treasurer, Dr. Lawrence Stream, Oklahoma City.

Personal.—Dr. Bert T. Brundage, of Thomas, has been appointed by Governor Raymond Gary a member of the state board of health to succeed Dr. Roy L. Fisher, of Frederick, who has resigned.—Dr. Gilbert S. Campbell, former assistant professor of surgery, University of Minnesota Medical School, has been appointed professor of surgery at the University of Oklahoma Medical School and chief of surgical service at the Oklahoma City Veterans Administration Hospital, Oklahoma City. As surgery chief at the hospital, he succeeds Dr. Fred A. Quenzer, who transferred to the McKinney, Texas, VA hospital last May.

PENNSYLVANIA

Nutrition Education Programs.—The commission on nutrition of the Medical Society of the State of Pennsylvania, under the chairmanship of Dr. Michael G. Wohl, Philadelphia, in cooperation with the National Vitamin Foundation, will present at the monthly meeting of various county medical societies, discussions on the basic and practical aspects of nutrition as they relate to disease. Several of these discussions have already been held and the remaining ones will be held as follows: Before the Delaware County Medical Society in Media, November 13, Willard Krehl, Ph.D., New Haven, Conn., will discuss "General Therapeutic Nutrition with Emphasis on Arthritic Disease"; be-

fore the Northampton County Medical Society at Easton, November 18, Robert W. Hillman's (Brooklyn) subject will be "Treatment of Obesity with Particular Reference to Nutrition"; before the Lancaster County Medical Society, Lancaster, December 3, Dr. Richard W. Vilter, Cincinnati, will speak on "Nutritional and Metabolic Aspects of Cardiovascular Disease"; the two objectives of this program being to stimulate interest in clinical nutrition at state and county levels and to disseminate factual information on nutrition to practicing physicians and the laity; and before the New Jersey Academy of General Practice in Atlantic City, January 10, 1959, Dr. Norman H. Jolliffe, New York City, will discuss "Fats, Cholesterol and Atherosclerosis—a Progressive Report."

Society News.—At a meeting of the Pittsburgh Roentgen Society the following officers were elected for 1958-1959: president, Dr. Harrison H. Richardson, Rochester; vice-president, Dr. Eugene R. Kutz, Pittsburgh; secretary, Dr. Erwin Beck, 3500 Fifth Avenue, Pittsburgh 13; and treasurer, Dr. Julius W. Ambrose, Pittsburgh.

RHODE ISLAND

The Danforth Oration.—Dr. Paul C. Colonna, until recently professor of orthopedic surgery, University of Pennsylvania School of Medicine, Philadelphia, will serve as orthopedic surgeon-in-chief pro tempore at the Rhode Island Hospital, Nov. 6-8. On Nov. 6 he will deliver the Murray S. Danforth Oration on "The Ununited Hip."

SOUTH CAROLINA

Society News.—The South Carolina Chapter of the American Academy of General Practice has installed the following officers: president, Dr. Homer M. Eargle, Orangeburg; president-elect, Dr. I. Ripon Wilson, Charleston; vice-president, Dr. William T. Hendrix, Spartanburg; and secretary-treasurer, Dr. Horace M. Whitworth, Greenville.

Personal.—Dr. Kenneth M. Lynch Jr., dean of the faculty of the Medical College of South Carolina, Charleston, has been honored by award of the "Medallion and Citation" of the American Cancer Society for "outstanding service in the cause of cancer control." The award was made at the South Carolina Division's annual meeting April 1.——Dr. Hugh S. Brown, for the past nine years has maintained a private practice in Spokane, Wash., as a specialist in internal medicine and cardio-vascular diseases, has been appointed medical director of Liberty Life Insurance Company, succeeding Dr. W. S. Fewell, who has retired.

TEXAS

Hospital News.—A grant of $52,000 for a study of how electronic data processing equipment may best be adapted for hospital use has been made by The John A. Hartford Foundation to the Hospital Research and Educational Trust. Dr. Edwin L. Crosby, chairman, board of trustees of the trust, said the study would require about four months and would be carried out in Dallas, at the Baylor University Hospital. The study will include the areas of patients' billings, perpetual inventories, medical records and statistics, payroll and insurance. The Hospital Research and Educational Trust, a nonprofit organization, with grants from foundations and other sources, conducts projects for general improvement of knowledge and practice in the hospital field.

Personal.—Dr. Cyril J. Ruilmann, director of mental health and hospitals, Board for Texas State Hospitals and Special Schools, has been elected chairman of the Southern Regional Council on Mental Health Training and Research, for 1958-59.——Dr. Kenneth M. Earle, associate professor of pathology, University of Texas Medical Branch, Galveston, has been made assistant dean (undergraduate) and Dr. Stephen R. Lewis, assistant professor of surgery at the University of Texas Medical Branch, has been made assistant dean (graduate and postgraduate).——Dr. Herschel F. Connally has been appointed assistant executive director of the Medical Branch of the University of Texas, Galveston. Dr. Connally has been a member of the Commission on Higher Education for the State of Texas.

VERMONT

State Medical Election.—At the annual meeting of the Vermont State Medical Society in Bretton Woods, New Hampshire, in September, Dr. Wayne Griffith of Chester was installed as president and the officers elected were : Dr. Frederick W. Van Buskirk, Burlington, president-elect; Dr. Benjamin F. Clark, St. Johnsbury, vice-president; Dr. Oliver H. Durand, Bennington, secretary; Dr. Gordon B. Smith, Rutland, treasurer; and Dr. William J. Powers, Rutland, speaker of the house.

The following were awarded memberships in the 50-year club: Drs. Benjamin D. Adams, Burlington; Oliver N. Eastman, Burlington; Arthur T. Gillette, Dorset; Archie L. Leonard, Lyndonville; William McFarland, Barre; and John H. Woodruff, Barre.

The annual meeting next year will again be a joint meeting with the New Hampshire Medical Society at the Equinox House in Manchester, Vermont, October 1-4.

WASHINGTON

State Medical Election.—At the annual meeting of the house of delegates of the Washington State Medical Association in Spokane, September 17, the following officers were elected: Dr. Emmett L. Calhoun, Aberdeen, president; Dr. Frederick A. Tucker, Seattle, president-elect; Dr. Milo T. Harris, Spokane, immediate past-president; Dr. Edward C. Guyer, Seattle, vice-president; Dr. Wilbur E. Watson, Seattle, secretary-treasurer; and Dr. Homer W. Humiston, Tacoma, speaker, house of delegates.

GENERAL

22,880 Traffic Deaths in Eight Months.—A forecast by the National Safety Council, Chicago, September 30, was to the effect that a saving of 2,000 lives on the nation's highways in 1958 is a realistic goal. The council based its forecast on the fact that the traffic death toll of 22,880 for the first eight months of this year is 6% below the same period last year.

For the eight months, 32 states had better records than for the same period the year before and 186 cities still had perfect records, the three largest being Orlando, Florida, Evanston, Illinois and Bethlehem, Pennsylvania.

Society News.—The American Academy of Physical Medicine and Rehabilitation has elected the following officers for 1958-59; Dr. Louis B. Newman, Chicago, president; Dr. Clarence W. Dail, San Gabriel, Calif., president-elect; Dr. Ray G. Piaskoski, Wood, Wis., vice-president; Dr. Harriet E. Gillette, Atlanta, Ga., secretary; Dr. James W. Rae Jr., Ann Arbor, Mich., treasurer; and Dorothea C. Augustin, Chicago, executive secretary.

Regional Meeting of College of Physicians.—The regional meeting of the American College of Physicians (New England states, Quebec, and Atlantic Provinces) will be at the Chateau Frontenac Hotel, Quebec, Canada, November 7-8, to which a cordial invitation is extended to all physicians of these regions. There will be no registration fee. In addition to the scientific session, at the banquet Friday evening, Dr. Dwight L. Wilbur, San Francisco, president, American College of Physicians; Monseigneur A. M. Parent, rector of Laval University; and Edward R. Loveland, Philadelphia, executive secretary of the college, will be the guests of honor. The ladies' program includes a luncheon, tour of old Quebec and Laval University, and a visit to the shrine of Saint Anne de Beaupre.

Surgeons' Election.—Dr. Henry W. Meyerding, of Rochester, Minn., was inducted as president of the International College of Surgeons at ceremonies in the Palmer House, Sept. 19, succeeding Dr. Carlos Gama of Sao Paulo, Brazil. Other officers installed were: Dr. A. Mario Dogliotti of Torino, Italy, president-elect, to take office as president in 1960; Dr. Lyon H. Appleby, Vancouver, B. C., first vice-president; Dr. Max Thorek, Chicago, secretary-general; Dr. Ross T. McIntire, Chicago, executive director; Dr. Clement L. Martin, Chicago, treasurer. Dr. Edward L. Compere, Chicago, was installed as president of the United States Section, succeeding Dr. Curtice Rosser, Dallas. Dr. Harry E. Bacon, Philadelphia, was inducted as president-elect, and Dr. A. Neal Owens, New Orleans, as first vice-president.

Meeting of Tropical Medicine Society.—The seventh annual meeting of the American Society of Tropical Medicine and Hygiene will be Nov. 5-8 at the University of Miami School of Medicine, Coral Gables. In addition to scientific papers by local and South American scientists, the 23rd annual Charles F. Craig lecture will be given by Dr. Jerome T. Syverton, University of Minnesota Medical School, Minneapolis. At the dinner Friday evening, the presidential address will be delivered by Donald L. Augustine, Sc.D., Waban, Mass., of the Harvard School of Public Health, on "The Worm Turned—Action and Reaction." The Walter Reed Medal will be presented by Willard H. Wright, Ph.D., Washington, D. C., chairman of the award committee. The next annual meeting will be in Indianapolis October 28-31, 1959.

Conference on Lead Hygiene in Chicago.—The Lead Industries Association, New York City, will present a Lead Hygiene Conference at the Drake Hotel, Chicago, Nov. 6-7. Chairmen of the three sessions will be Dr. Lemuel C. McGee, Dr. George M. Wheatley and Mr. Manfred Bowditch, director of health and safety of the association. Speakers and subjects will include the following:

Effect of Environmental Temperature on Lead Poisoning, Anna M. Baetjer, Sc.D., Baltimore.
Health Control in Storage Battery Manufacture, Dr. Elston L. Belknap, Milwaukee.
Studies of the Lead Content of Waters from Red Lead Painted Standpipes, Dr. Higdon B. Elkins, Iowa City, Iowa.
Common Errors in the Diagnosis of Plumbism, Dr. Rutherford T. Johnstone, Los Angeles.

Attendance is limited to 150 persons. Registration fee for members is $10. For information write the Lead Industries Association, 60 E. 42nd St., New York 17, New York.

Recipients of Pediatric Fellowships.—The recipients of the annual Wyeth Laboratories pediatric residency fellowships have been announced by Dr. Philip S. Barba, past-president of the American Academy of Pediatrics and chairman of the fellowship selection committee. The physician-recipients, from 13 different states, are the first group to benefit from this fellowship program established recently. Each will receive a grant of $4,800 providing for a

two-year postgraduate course in pediatrics. The cost of the first three years of the project will be $195,000. Those receiving the fellowship awards included:

Drs. Sidney W. Klein, Baltimore, Md.; Robert B. Cole, Cleveland, Ohio; Floy C. Helwig, Baltimore; Warren D. Grover, Camp LeJeune, N. C.; Luther B. Travis, Fort Benning, Ga.; John D. Siegfried, Red Lake, Minn.; George T. Kimbrough, Birmingham, Ala.; Donald E. Carey, New Orleans, La.; Marvin L. Rallison, Minneapolis; Allan L. Drash, Baltimore; William G. Kenney, Rochester, N. Y.; Paula Neyman, New York City; Keith Hammond, Paoli, Ind.; Robert O. Hickman, Salt Lake City; John C. Gilliland, Jackson, Miss.; Jon L. Karlsson, Santa Rosa, Calif.; John I. Larkin, Albany, N. Y.; William A. Moon Jr., Denver; George A. Lentz, Baltimore; and Paul J. Uhlig, Oceanside, Calif.

Essay Contest on Maxillofacial Surgery.—The American Society of Maxillofacial Surgeons has announced an essay contest for papers based on some original research (either clinical or experimental) in maxillofacial surgery. Any medical or other university graduate may enter. The essays shall be based on work not previously published, even in part, and shall be submitted in triplicate, in English only, and not more than 4,000 words in length. Manuscripts will not be accepted by the Award Committee after April 1, 1959, and should be sent by registered mail. Certificates will be given to the authors of the first and second prize essays. The winners of these certificates will receive $300 and $200, respectively for travelling expenses. The two winning papers are to be read by the authors before the annual convention of the society, May 10-14, 1959, at the Palmer House, Chicago. The submitted essay becomes the property of the American Society of Maxillofacial Surgeons and shall not be published, without the written permission of the Secretary of the Society, in any journal other than the official journal of the Society, *The American Journal of Surgery*. Information may be obtained from the Secretary of the Society, Dr. Orion H. Stuteville, 700 N. Michigan Ave., Chicago 11.

New Journals of Pharmacology.—Three new journals of pharmacology have been announced. *Biochemical Pharmacology*, an international journal devoted to research into the development of biologically active substances and their mode of action in the biochemical and subcellular level, is edited by a board of which Dr. Alexander Haddow, of the Chester Beatty Research Institute, is chairman. The regional editor for the United States is Dr. Arnold D. Welch, of Yale University, New Haven, Conn. The first volume appeared in July. The Academic Press, Inc., of New York City, has announced the publication of *Toxicology and Applied Pharmacology* with Harry W. Hays, Ph.D., of the National Research Council, as managing editor, assisted by Frederick Coulston, Ph.D., of the Sterling-Winthrop Institute, and Dr. Arnold J. Lehman, of the Food and Drug Administration. The first number is to appear in January, 1959. Interscience Publishers, of New York City, have announced an international bimonthly periodical, *Journal of Medicinal and Pharmaceutical Chemistry*, the first issue to appear toward the end of the year. This will have as editors Mr. Arnold H. Beckett, of the Chelsea College of Science and Technology, London, and Alfred Burger, Ph.D., of the University of Virginia, Charlottesville.

Awards for Research in Radiology.—On behalf of the James Picker Foundation, The National Academy of Sciences–National Research Council announces the continued availability of funds in support of radiological research. The program is oriented toward, but not necessarily limited to, the diagnostic aspects of radiology. Support is not restricted to citizens of the United States or to laboratories within this country. Three types of support are offered: (1) grants-in-aid, designed to encourage investigations offering promise of improvement in radiological methods of diagnosis or treatment of disease, awarded to institutions, rather than to individuals; (2) grants for scholars, designed to bridge the gap between the completion of fellowship training and the period when the young scientist has demonstrated his competence as an independent investigator, applied for by the institution on behalf of the prospective scholar; (3) fellowships in radiological research open to candidates seeking to gain research skills leading to investigative careers in the field of radiology. Candidates must hold the M.D., Ph.D., or Sc.D. degree or the equivalent. Preference will be given to applicants who are 35 years of age or less. Applications for the fiscal year 1959-1960 should be submitted by Dec. 1. Information and application blanks may be obtained from the Division of Medical Sciences, Room 411, National Academy of Sciences–National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C. Applications for support of studies to be carried out in Canada should be directed to the Awards Office, National Research Council of Canada, Ottawa 2, Canada.

Outbreaks of Infectious Encephalitis.—According to the Morbidity and Mortality Weekly Report of the United States Public Health Service, dated September 26, 1958, a total of 116 cases of infectious encephalitis was reported for the current week; 30 in Kansas, 17 in California, 10 in Georgia, 9 in Nebraska, 7 in Ohio, and 6 in Texas. The report for Kansas showed that 1 of the 30 had been confirmed as western equine and 1 as St. Louis encephalitis, 2 as mumps encephalitis, and 26 as unknown etiology. Four cases reported as "meningococcal encephalitis" were placed in the category of meningococcal infections.

The California Department of Public Health reports that 3 new cases of arthropod-borne encephalitis were confirmed during the 2-week period ended September 18. In the 2 preceding 2-week periods 12 and 10 cases had been confirmed. The 3 new cases were diagnosed as western equine encephalitis infections, making a total of 31 confirmed cases of this disease. Three cases of St. Louis encephalitis have been confirmed this year. One of the 3 cases of western equine encephalitis was presumably contracted in Santa Clara County, which is outside of the usual endemic area for arthropod-borne encephalitis, but the individual was reported to have been in Utah during the summer although the exact dates of his stay were not known.

The Colorado Communicable Disease Summary for the week ended September 6 contains a report that 4 cases of arthropod-borne encephalitis have been confirmed as the western equine type. Four other cases have been ruled out by laboratory tests as cases of arthropod-borne encephalitis.

Competition for Treatise on Rheumatic Diseases.—The 4th International Award AQUI TERME (Hot Springs) of Rheumatology, under the auspices of the Italian Society of Rheumatology, has been announced. The international competition is for a prize for an unpublished treatise on the rheumatic disease (award 1,000,000 lire [$1,600]) and for a publication in the form of a composition or monograph on the subject of rheumatology (award 500,000 lire).

Rules are as follows:

Treatises seeking the prize of lire 1,000,000 must discuss problems involving the articular physiopathology, the clinical aspects or treatment of the arthritic or rheumatic diseases.

Publications seeking the prize of lire 500,000 must discuss rheumatologic arguments in a form of a composition or monograph.

This competition is open to all Italian and foreign physicians.

The prize of Lire 1,000,000 might be awarded to one publication or divided between two publications. The prize of lire 500,000 is indivisible.

The committee of award will consist of six authorities on rheumatic and arthritic diseases.

The jury will have the right to cancel this competition if in its judgment the quality of the publications will not be up to standards.

Publications may be written in Italian, French, English, German, or Spanish. It is desirable to make an abstract of the publication in either Italian or French.

Publications must be counter-signed with a motto; the same motto must be repeated on the sealed envelope on which the following indications must be written: motto, the name and address of the author or authors.

Publications must be typewritten (for award of lire 1,000,000); typewritten or printed (for award of lire 500,000) and send in 8 copies, postage prepaid and insured to: Azienda Autonoma di Cura di Acqui Terme (Piemonte, Italy).

The closing date of the competition is December 31, 1958.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Medical schools in the United States and Foreign Countries, Feb. 17 and Sept. 22. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

CALIFORNIA: *Oral Examination.* San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

COLORADO: *Endorsement.* Denver, Oct. 14. *Written.* Denver, Dec. 9-10. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

MAINE: *Examination and Reciprocity.* Portland, Nov. 12-14. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Nov. 17-18. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

OHIO: *Examination.* Columbus, Dec. 16-18. *Endorsement.* Columbus, Dec. 16-18. Sec., Dr. H. M. Platter, Wyandotte Bldg., Columbus 15.

SOUTH CAROLINA: *Endorsement.* Columbia, Dec. 9. Sec., Dr. H. E. Jervey, Jr., Blanding Bldg., Columbia.

TEXAS:* *Examination and Reciprocity.* Fort Worth, Dec. 4-6. Sec., Dr. M. H. Crabb, 1714 Medical Arts Building, Fort Worth 2.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

DISTRICT OF COLUMBIA: *Reciprocity. Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

KANSAS: *Examination and Reciprocity.* Kansas City, Nov. 24-25. Sec., Dr. L. C. Heckert, Pittsburg.

OKLAHOMA: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

TEXAS: Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Milwaukee, Dec. 6, Madison, Apr. 4. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

Colonel Benford Named Director of Medical Publication Agency.—Col. Robert J. Benford, M. C., has been named director of the Armed Forces Medical Publication Agency and editor of the *U. S. Armed Forces Medical Journal*. He succeeds Capt. Bennett F. Avery, M. C., U. S. N., who has been appointed national coordinator of the Medical Education for National Defense program.

Colonel Benford, who recently completed a tour of duty in the Office of the Assistant Secretary of Defense (Health and Medical), served as staff surgeon of the XX Bomber Command in World War II. He is a member of the editorial advisory board of *Aero/Space Engineering*, a monthly journal of the Institute of Aeronautical Sciences, and the author of "Doctors in the Sky," a history of aviation medicine.

General Harry Armstrong Retires.—Major Gen. Harry G. Armstrong, formerly surgeon general of the U. S. Air Force, retired Sept. 1, after almost 30 years of military service. While commandant of the School of Aviation Medicine, he established, on Feb. 9, 1949, the first Department of Space Medicine. In 1935 he was the first physician to attempt a delayed opening parachute jump, of which a report was published in THE JOURNAL, Oct. 5, 1935. He was the first to recognize explosive decompression as one of the most hazardous problems in the use of pressurized cabins and, in many of those experiments, he himself was the test subject.

General Armstrong received a Master of Arts degree in internal medicine from the University of Cincinnati and a Master of Science degree in physiology from the University of Toronto. He was elected president of both the Aero Medical Association and the Association of Military Surgeons in 1951. For the past three years he has been surgeon of the U. S. Air Forces in Europe.

ARMY

Personal.—On Oct. 1, Col. Howard W. Doan, M. C., became surgeon of the First Army, with headquarters at Governors Island, New York, succeeding Brig. Gen. Roger G. Prentiss who retired on Sept. 30. Colonel Doan's previous assignment was deputy commander of the Fitzsimons Army Hospital in Denver.

General Prentiss Retires.—Brig. Gen. Roger G. Prentiss, surgeon of the First Army with headquarters at Governors Island, New York, retired Sept. 30, after more than 30 years' service as a medical officer. When World War II broke out, General Prentiss was called to the surgeon general's office in Washington, D. C., to become director of medical research and development. Later he went to Europe with a special intelligence team whose mission was to enter captured German towns to collect data on technical advances by the Germans. In 1950 he became chief of the Historical Division in the surgeon general's office and in 1951 executive officer of the surgeon general's office. At a parade in his honor on Sept. 24, First U. S. Army Commander, Lieut. Gen. B. M. Bryan, presented to General Prentiss the second award of the Legion of Merit. General and Mrs. Prentiss plan to make their home in Florida.

Establish Medical Research and Development Command.—The surgeon general's office has announced the activation of the Army Medical Service's new Research and Development Command. Brig. Gen. Joseph H. McNinch has been appointed Commanding General of the new command and will assume his duties about Nov. 1. General McNinch is returning to Washington from his post as surgeon, Armed Forces Far East, U. S. Eighth Army, Japan.

Research studies with which the new command will be concerned include the medical effects of ionizing radiation; the prevention and treatment of communicable diseases in overseas areas; surgical problems in the care of the burned and wounded; medical problems of operations under temperature extremes and other adverse environmental conditions; and the physiological and neuropsychiatric problems of military operations.

NAVY

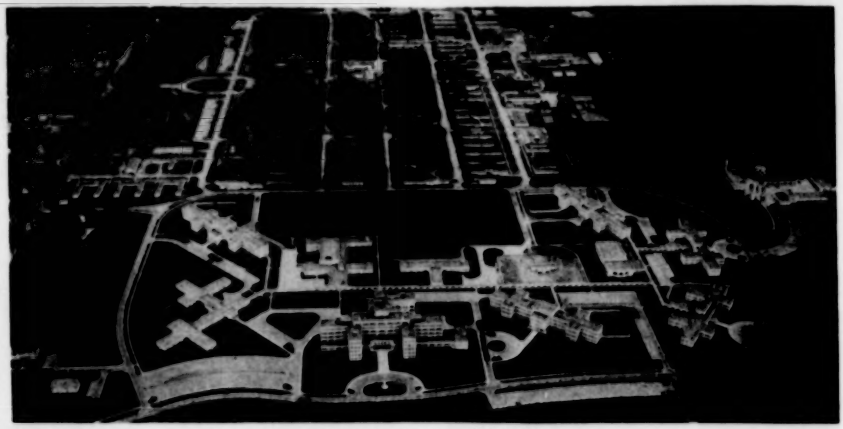
Medical Corps Retirements.—Capt. William W. Ayres, M.C., was placed on the retired list on Sept. 1, 1958, after completing more than 20 years' active service. Having been specially commended by the head of the executive department for his performance of duty in actual combat, he will be advanced on the retired list to the rank of rear admiral.

Capt. Victor G. Colvin, M.C., was placed on the retired list on Sept. 1, after completing more than 27 years' active service.

Capt. Thomas M. Foley Jr., M. C., was placed on the retired list on Sept. 1, after completing more than 20 years' active service.

VETERANS ADMINISTRATION

Proposed Neuropsychiatric Hospital at Brecksville, Ohio.—The VA announced Sept. 19 that bids will be accepted up until Nov. 4 for the construction of an estimated $20,500,000 veterans' hospital at Brecksville, Ohio. Aside from the buildings to be constructed, the project includes roads, walks, drainage, landscaping, grading, and wrecking and removal of certain existing structures. In general, the buildings will have concrete and steel frames, reinforced concrete foundations and floors, and exterior brick and masonry walls with stone trim and built-up roofs. Specifications are available from the Director, Design Service, Veterans Administration, Munitions Building, Washington 25, D. C.



Veterans Administration Hospital, Topeka, Kan.

The Sixtieth Hospital Since World War II.—The Veterans Administration dedicated a new 1,011-bed hospital for neuropsychiatric patients on Aug. 24, at Topeka, Kan. This, the 60th VA hospital built since World War II, replaces the temporary structures built for the Army in 1943 and later turned over to the Veterans Administration. The new hospital is on Gage Boulevard, three miles from the center of Topeka, on a site of about 150 acres. The hospital proper comprises about 20 buildings of reinforced concrete, with brick facing. The cost of construction approximated 20 million dollars. It will be staffed by about 1,150 employees. Among the speakers at the dedication were Dr. Karl A. Menninger of Topeka and Dr. William S. Middleton, VA chief medical director. The U. S. Army Band from Fort Riley, Kansas, provided music, and Mr. David Neiswanger, chairman, Executive Committee, Menninger Foundation, was master of ceremonies.

Personal.—Dr. Edward F. Zimmerman, director, professional services, VA hospital, Coral Gables, Fla., has been appointed manager of the West Side VA Hospital in Chicago, succeeding Dr. Lee H. Schlesinger, who was appointed VA area medical director at Columbus, Ohio. The West Side hospital is a 495-bed facility for general medical and surgical patients. Dr. Louis B. Newman, chief, physical medicine and rehabilitation service, VA Research Hospital, Chicago, has been presented the agency's Meritorious Service award. Dr. Newman was cited for outstanding service in organizing the research hospital's physical medicine and rehabilitation service and the VA center for rehabilitation of blinded veterans at the Hines, Ill., VA Hospital. Dr. Newman is president of the American Academy of Physical Medicine and Rehabilitation. Dr. A. W. Kruger, formerly manager of the Brooklyn, N. Y., VA Hospital, has resigned from the Veterans Administration to accept the post of consultant on health services to the National Committee on Aging of the National Social Welfare Assembly, 345 E. 46th St., New York City.

PUBLIC HEALTH SERVICE

Research Grants Awarded in July and August.—Research grants and fellowships totaling $42,665,767 were awarded during the months of July and

August by the National Institutes of Health, Bethesda, Md. In all, 2,793 grants were made to 489 institutions in 48 states, the District of Columbia, 2 territories, and 12 foreign countries. More than half of the money went for the support of research projects concerned with allergy, infectious diseases, heart disorders, and various basic problems in the medical and biological sciences. About one-third of the total number of grants were for new projects, of which 224 are in the field of biological sciences basic to medicine.

Two and One-half Billion Dollars Spent on Hospital Construction.—In a publication on the nation's health facilities, just issued by the Public Health Service, is a summary of the Hill-Burton program up to Jan. 1, 1958. During the first 10 years of the program, 3,047 projects—general hospitals, nursing homes, diagnostic and treatment centers, rehabilitation facilities, public health centers, and state health laboratories—were approved for construction. Of the total cost of 2.5 billion dollars, the state and local share was nearly 1.7 billion. The number of people in the United States without ready access to general hospitals has dropped from 10,000,000 to 2,800,000 since 1948, the Public Health Service reported.

More Than 9,000 Grants in One Year.—The National Institutes of Health, Bethesda, Md., awarded 9,534 grants for research, training, and construction in nonfederal institutions during the fiscal year ended June 30. Of the total, $136,112,014, more than two-thirds—$99,480,968—went to support 7,028 research projects concerned with major diseases and problems in the medical and biological sciences. The grants were made to 699 institutions in 48 states, the District of Columbia, 2 territories, and 28 foreign countries. Grants to help build, equip, or expand 177 research facilities, totaling $30,200,095, were awarded on a matching basis to 134 institutions throughout the country. Research fellowships totaling $6,430,951 were awarded to 2,329 fellows. Eighty-four United States scientists were awarded fellowships for study abroad, while 16 scientists from other countries received fellowships for study in outstanding institutions in the United States.

Grant Support for Training in Psychiatry.—The National Institute of Mental Health is offering grant support for a training program for general practitioners and other physicians engaged in the practice of medicine other than psychiatry. Funds are available during the current year (fiscal year 1959) and training institutions may submit applications at any time. The program has two purposes:

1. To foster the development of postgraduate training in psychiatry for practitioners who wish to increase their psychiatric knowledge and skills in order to be able to deal more effectively with the emotional aspects of illness generally and to play a more effective role in the treatment and prevention of mental illness. These courses will be designed for the physician who plans to continue practicing in his own field.

Grant support is being offered to medical schools, hospitals, clinics, and medical and psychiatric societies for the development and expansion of such postgraduate training in the form of courses, institutes, and seminars. This support does not include fees, subsistence, or travel for the physicians who attend.

Support of this type of training may be for a particular professional group over a given period, or for training offered regularly as part of the postgraduate curriculum of a medical school, hospital, or clinic, or as part of the educational program of a medical or psychiatric society.

Physicians interested in obtaining this type of training should apply to medical schools, hospitals, clinics, and medical or psychiatric societies which have, or are developing, such training opportunities.

2. To provide support at an adequate level for psychiatric residency training for physicians in practice who wish to become psychiatrists. Training stipends up to a maximum of $12,000 a year are available. The level of payment will be determined by the training institutions who will also make the award to the individual physicians. The National Institute of Mental Health will make awards of grants for this purpose to training institutions and not to individuals.

Physicians interested in support for this type of training should apply to training institutions which are approved for psychiatric residency training.

Inquiries about the program should be sent to Dr. Seymour D. Vestermark, Chief, Training Branch, National Institute of Mental Health, Bethesda 14, Md.

SELECTIVE SERVICE

Physical Examination of Physicians for the Armed Forces.—The director of the Selective Service System, Lewis B. Hershey, issued the following operations bulletin on Sept. 22.

1. It is currently reported that too few physicians are volunteering for active duty and residency programs to meet service requirements.

2. If the present trend continues, the Selective Service System will be called upon to deliver physicians on a special call. Local boards will be expected, in anticipation of a possible special call for physicians (but not dentists), to proceed with the physical examination of all physicians who are in class I-A or class I-A-O and have not been examined or who are in class IV-F under the provisions of section 1622.44 (a) of the regulations.

3. Operations Bulletin no. 181, issued Aug. 19, 1957, on the subject "Postponement of Armed Forces Physical Examination and Induction of Physicians and Dentists," is being amended to discontinue the postponement of the examination and induction of physicians.

4. For the purposes of this bulletin a physician is any registrant who has received the degree of bachelor of medicine or doctor of medicine.

DEATHS

Ahroon, Carl Richard Jr. Ⓜ Bloomington, Ill.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1932; veteran of World War II; associated with St. Joseph's and Mennonite hospitals in Bloomington and Brokaw Hospital in Normal, where he died Aug. 25, aged 53, of coronary artery disease.

Ausban, Henley Brown Ⓜ Doyle, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1912; died July 19, aged 79.

Baldwin, Arthur Kirby Ⓜ Long Beach, Calif.; born in Berwick, Ill., July 12, 1888; Rush Medical College, Chicago, 1916; certified by the National Board of Medical Examiners; enlisted in the Army and served with the American Occupational Forces in Siberia in 1919 and 1920; member of the American Society of Anesthesiologists and the Illinois Society of Anesthesiologists; served four times as president of the Green County (Ill.) Medical Society; the Illinois State Medical Society selected him as "General Practitioner for 1958"; practiced in Carrollton, Ill., where he was associated with Carrollton Hospital; died in the Seaside Memorial Hospital May 12, aged 69, of carcinoma of the liver.

Bennett, Marion Horton Ⓜ Big Spring, Texas; Tulane University School of Medicine, New Orleans, 1921; veteran of World War I; chief of staff, Howard County Hospital Foundation; died Aug. 25, aged 63, of ventricular fibrillation.

Booher, James Mathew, Chicago; Kentucky University Medical Department, Louisville, 1905; died in the Manteno (Ill.) State Hospital May 12, aged 78.

Bowman, James Luther Ⓜ Montgomery, Ala.; University of Virginia Department of Medicine, Charlottesville, 1897; served as secretary-treasurer of the Montgomery County Medical Society; veteran of World War I; formerly county health officer; for many years assistant head of the Montgomery County Health Department; died Aug. 24, aged 84.

Calkins, Irving Romaro Ⓜ Springfield, Mass.; Baltimore Medical College, 1896; died Aug. 26, aged 82, of cerebral hemorrhage and mitral stenosis.

Case, Frank William, Cincinnati; Miami Medical College, Cincinnati, 1907; member of the Ohio State Medical Association; served as resident physician at the Christ Hospital where he died Aug. 25, aged 76.

Ⓜ Indicates Member of the American Medical Association.

Chalfant, Estalee Martha, Shinnston, W. Va.; Illinois Medical College, Chicago, 1904; American College of Medicine and Surgery, Chicago, 1905; died in Clarksburg Aug. 19, aged 89.

Dahlstrom, Arthur William, Albuquerque, N. M.; Marquette University School of Medicine, Milwaukee, 1916; member of the American Trudeau Society; joined the U. S. Bureau of Indian Affairs in 1935; served as special physician at large for the Indian Service, and as superintendent of the Indian Sanitarium; died Aug. 26, aged 68, of bilateral subdural hematoma and arteriosclerosis.

Daley, Thomas Robert, Oakland, Calif.; University of Wisconsin Medical School, Madison, 1951; interned at the Highland-Alameda County Hospital, where he served a residency; served a residency at the Samuel Merritt Hospital in Oakland and the Herrick Memorial Hospital in Berkeley; associated with the Veterans Administration Hospital; died Aug. 30, aged 33, in an automobile accident near Winters.

Ekstrom, John E., Chicago; Rush Medical College, Chicago, 1909; for many years on the staff of the Ravenswood Hospital; died in the Burnham City Hospital in Champaign Aug. 24, aged 75.

Gaberman, Peter Ⓜ Los Angeles; born in Odessa, Russia, Feb. 28, 1904; University of Illinois College of Medicine, Chicago, 1928; formerly practiced in Chicago, where he was associate professor of medicine at the Chicago Medical School, and on the staffs of the Cook County and Mount Sinai hospitals; veteran of World War II; member of the Illinois State Medical Society and the American College of Cardiology; specialist certified by the American Board of Internal Medicine; died in Cedars of Lebanon Hospital Sept. 7, aged 54, of acute coronary thrombosis with myocardial infarction.

Gault, Edwin Sartain Ⓜ Philadelphia; born in Philadelphia Dec. 23, 1893; Hahnemann Medical College and Hospital of Philadelphia, 1920; on the faculty of Temple University School of Medicine; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists; fellow of the College of American Pathologists; consultant for the U. S. Public Health Service; joint author of "Essen-

tials of Pathology"; associated with Episcopal Hospital and the Temple University Hospital, where he died Sept. 1, aged 64.

Goff, William Hunter ⊗ Rockford, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1935; served as health officer of Coosa County; died July 15, aged 50, of coronary occlusion.

Grant, John Joseph ⊗ Freeport, Ill.; University and Bellevue Hospital Medical College, New York City, 1911; past-president of the Stephenson County Medical Society; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War I; served as president of the medical staff at St. Francis Hospital, where he died Aug. 23, aged 72.

Gray, Robert, Philadelphia; Temple University School of Medicine, Philadelphia, 1912; died May 1, aged 79, of pulmonary embolism and rheumatic heart disease.

Greene, George A., Yates Center, Kan. (licensed in Kansas in 1901); died in the Newton Memorial Hospital, Winfield, Aug. 22, aged 85, of diabetes mellitus, bronchopneumonia, and congestive heart failure.

Hardesty, Henry O. ⊗ Jennings, Kan.; Kansas Medical College, Topeka, 1900; served overseas during World War I; died Aug. 17, aged 88, of coronary artery disease.

Heyroth, Francis Farnham ⊗ Cincinnati; University of Cincinnati College of Medicine, 1925; associate professor of industrial health and biological chemistry at his alma mater, where he received his Ph.D. in 1929; retired as assistant director of the Kettering Laboratory at his alma mater; formerly vice president of the Cincinnati Board of Health; a member of the National Advisory Dental Research Council of the U. S. Public Health Service; a member of the American Chemical Society which in 1953 presented him with its fourth annual Eminent Chemist Award; died Aug. 18, aged 63, of cerebral hemorrhage and hypertension.

Hill, Ralph Lee, Alexander, Va.; born July 6, 1876; Medical Department of the Western University of Pennsylvania, Pittsburgh, 1900; an associate member of the American Medical Association; past-president of the Pennsylvania Psychiatric Society; specialist certified by the American Board of Psychiatry and Neurology; past-president of the Berks County (Pa.) Medical Society and the Pennsylvania Psychiatric Society; member of the American Psychiatric Association; veteran of World War I; medical superintendent of the Allegheny County Home and Hospital in Woodville, Pa., from 1914 to 1927 and the Wernersville (Pa.) State Hospital from 1927 to 1954; in 1940 received an honorary doctor of science degree from Franklin and Marshall College, Lancaster, Pa.; died in the Jamestown (N. Y.) Hospital Aug. 22, aged 82, of uremia.

Howell, Asa, Uvalde, Texas; University of the South Medical Department, Sewanee, Tenn., 1899; died May 19, aged 85.

Hurd, Annah ⊗ Minneapolis; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1900; died July 24, aged 86.

Hurd, Laura B., San Francisco; Hahnemann Medical College of the Pacific, San Francisco, 1897; served on the staff of the Hahnemann Hospital, where she died Aug. 31, aged 88, of pulmonary embolism.

Hydrick, John Lee, Phoenix, Ariz.; born Oct. 25, 1888; Jefferson Medical College of Philadelphia, 1915; field representative of the Rockefeller Foundation in New York City from 1916 to 1953 and worked extensively in South American countries; a member of the World Health Organization expert advisory panel on health education of the public, and received decorations from the Netherlands, Peru, and Ecuador governments; on Sept. 1, 1956 was appointed acting city health director and the following year became co-director of the city and county health department; in 1954 received an honorary degree of doctor of law from Wofford College, Spartanburg, S. C.; died Aug. 29, aged 69.

Ingarra, Thomas Salvatore ⊗ Kingston, N. Y.; New York University College of Medicine, New York City, 1949; fellow of the American Society of Anesthesiologists; in 1955 served in the Army, stationed at Fort Riley, Kan., as chief of the department of anesthesiology until 1957; on the staffs of the Kingston Hospital and the Benedictine Hospital, where he died Aug. 28, aged 40, of lymphosarcomatosis.

Kauffman, Kalman L. ⊗ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1938; died Aug. 16, aged 46.

Kavaler, Samuel, Brooklyn; Long Island College Hospital, Brooklyn, 1922; member of the Medical Society of the State of New York; died Aug. 1, aged 64, of coronary occlusion.

Kavle, Carleton Porter ⊗ Niagara Falls, N. Y.; University of Buffalo School of Medicine, 1932; also a graduate in pharmacy; president of the Niagara County Medical Society; associated with Mount St. Mary's Hospital and the Memorial Hospital, where he died Aug. 24, aged 57, of hepatitis.

Key, William Frank ⊗ Fort Worth, Texas; Baylor University College of Medicine, Dallas, 1919; died Aug. 23, aged 67, of arteriosclerotic heart disease.

Mackey, Robert Bliss, Springville, Pa.; Medico-Chirurgical College of Philadelphia, 1908; veteran of World War I; died Aug. 25, aged 74, of rupture of an aneurysm of the abdominal aorta.

McDonald, John Thomas ⊗ Monroe, Tenn.; University of Nashville Medical Department, 1900; died in the Lady Ann Hospital in Livingston July 24, aged 90.

McGarry, Thomas Francis, Rutland, Vt.; University of Vermont College of Medicine, Burlington, 1921; associated with the Rutland Hospital; died Aug. 19, aged 61, of myocarditis.

McLean, Hugh Clayton, San Diego, Calif.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1903; served in the Canadian Army during World War I; died Aug. 14, aged 90, of arteriosclerosis.

Marsh, Charles Lafayette ⊗ Valley, Neb.; University of Nebraska College of Medicine, Omaha, 1941; member of the American Academy of General Practice; for 15 years a member of the Selective Service System; served on the District 33 board of education; on the staff of the Nebraska Methodist Hospital in Omaha; died in Portland, Ore., Aug. 26, aged 45, of fatty degeneration of the liver.

Mentzer, John F. ⊗ Ephrata, Pa.; Jefferson Medical College of Philadelphia, 1882; on the staff of the Ephrata Community Hospital; for many years trustee of the Harrisburg (Pa.) State Hospital; served as a member of the board of health, school director, postmaster, deputy coroner, and county treasurer; chairman of the board of directors and past-president of the Ephrata Farmers National Bank; died Aug. 28, aged 96, of cerebral thrombosis.

Michaelis, Lucia ⊗ Shaker Heights, Ohio; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1922; died in the Mount Sinai Hospital Aug. 19, aged 61.

Monk, Louis, New York City; Fordham University School of Medicine, New York City, 1911; an associate member of the American Medical Association; died in the Royal Hospital July 25, aged 81, of coronary thrombosis and arteriosclerosis.

Morris, Benjamin Franklin, Paducah, Ky.; Louisville (Ky.) Medical College, 1898; also a druggist; died in Riverside Hospital, Aug. 16, aged 81, of cerebral hemorrhage.

Morris, Elliston Joseph, St. Davids, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1886; an associate member of the American Medical Association; for many years associated with the Episcopal Hospital in Philadelphia; died in Devon Aug. 31, aged 95.

Muller, Lula Johnson Power, Montclair, N. J.; University of Virginia Department of Medicine, Charlottesville, 1946; interned at the Lenox Hill Hospital in New York City and served a residency at St. Luke's Hospital in New York City; associated with Mountainside Hospital; died near Susanville, Calif, Aug. 28, aged 37, of injuries received in an automobile accident.

Murphy, Leonard J. ⊗ Chicago; Northwestern University Medical School, Chicago, 1916; veteran of World War I; retired in 1956 as director of the Murphy Clinical and X-Ray Laboratory; died in the Swedish Covenant Hospital Aug. 29, aged 76, of diabetes mellitus and arteriosclerosis.

Nelson, Cedric Henry ⊗ Billings, Mont.; University of Nebraska College of Medicine, Omaha, 1923; past president of Yellowstone Valley Medical Society; served as past-president and vice president of the state board of medical examiners; past chairman of District 2 School Board; veteran of World War I; since 1951 health officer; a staff member at St. Vincent and Deaconess hospitals; died Aug. 20, aged 61, of complications following surgery for aortic aneurysm three months previously.

Noyes, Harriett Louella ⊗ Rumford, Maine; College of Physicians and Surgeons, Boston, 1911; died in the Rumford Community Hospital July 18, aged 69, of sarcoma.

Parker, Rupert Merrill ⊗ Moline, Ill.; Northwestern University Medical School, Chicago, 1896; formerly practiced in Chicago; died in the Lutheran Hospital Aug. 28, aged 88, of injuries received in an automobile accident.

Pennell, Franklin Howard ⊗ Fostoria, Ohio; Ohio State University College of Medicine, 1920; associated with Fostoria City Hospital; died Aug. 17, aged 63, of coronary occlusion.

Poppen, Joseph A. ⊗ Burr Oak, Kan.; St. Louis University School of Medicine, 1908; served for many years on school boards in both Ionia and Burr Oak; at one time superintendent of schools at Glen Elder; on the staffs of Beloit (Wis.) Community Hospital and St. Joseph's Hospital, Concordia, where he died Aug. 16, aged 82, of cerebral hemorrhage.

Reed, Wendell Phillips ⊗ Buffalo; University of Buffalo School of Medicine, 1932; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; consulting urologist Wyoming County Community Hospital, Warsaw,

and Our Lady of Victory Hospital, Lackawanna; past-president of the medical staff, Millard Fillmore Hospital, where he died Aug. 20, aged 54.

Reeves, Emory West, Cotulla, Texas; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; veteran of World War I; died June 14, aged 79.

Rohr, Joseph ⊗ New York City; University and Bellevue Hospital Medical College, New York City, 1908; died July 20, aged 76, of coronary artery disease.

Runge, Otto Ernst, Ridgewood, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1914; died July 30, aged 69, of carcinoma of the rectum with metastasis to the liver and lungs and diabetes mellitus.

Sappington, William Fulford ⊗ Lieut., Colonel, U. S. Army, retired, Waco, Texas; University of Maryland School of Medicine, Baltimore, 1901; veteran of World Wars I & II; entered the medical corps of the U. S. Army in 1920; service member of the American Medical Association; retired March 31, 1942; died June 3, aged 79.

Schabinger, Charles, Philadelphia; Medico-Chirurgical College of Philadelphia, 1899; also a graduate in pharmacy; an associate member of the American Medical Association; died Aug. 24, aged 86, of pneumonia and arteriosclerosis.

Schwartz, William H., Houston, Texas; Dunham Medical College, Chicago, 1902; Hering Medical College, Chicago, 1904; died in St. Luke's Hospital May 19, aged 81.

Seth, Raymond Ephraim ⊗ Seattle; University of Minnesota Medical School, Minneapolis, 1929; member of the Industrial Medical Association; veteran of World War II; on the staff of the Swedish Hospital; died Aug. 24, aged 54, of a self-inflicted bullet wound in the head.

Slayton, Frederic Hosea, Wichita, Kan.; Rush Medical College, Chicago, 1901; served on the staff of the Wesley Hospital; died Aug. 14, aged 83, of heart disease.

Southard, Mabel Austin, Los Altos, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1900; died Aug. 5, aged 76, of coronary thrombosis.

Stout, Henry Isaiah ⊗ Sherman, Texas; George Washington University School of Medicine, Washington, D. C., 1907; on the staff of the Wilson N. Jones Hospital; died Aug. 29, aged 74, of acute myocardial infarction and arteriosclerosis.

Thompson, Joseph ⊗ Creedmoor, N. C.; Kentucky University Medical Department, Louisville, 1904; died Aug. 22, aged 76.

Tietze, Herman Christian, Edwardsville, Ill.; Bennett Medical College, Chicago, 1913; past-president of the Madison County Medical Society; veteran of World War I; died in the Veterans Administration Hospital, Jefferson Barracks, Mo., Aug. 24, aged 73.

Turner, Andrew Jackson ⊗ Garnett, Kans.; Kansas City (Mo.) Medical College, 1902; veteran of the Spanish-American War and World War I; died Aug. 4, aged 79, of chronic brain syndrome and cerebral arteriosclerosis.

Underwood, Robert Alfred ⊗ Delta, Colo.; College of Medical Evangelists, Loma Linda and Los Angeles, 1933; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; at one time city physician in Lincoln, Nebr.; on the staff of the Delta Memorial Hospital; died Aug. 17, aged 55, of coronary thrombosis.

Vaughan, Merritt Carlton ⊗ Buffalo; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1911; associated with Deaconess, Millard Fillmore, Sisters of Charity, and Lafayette General hospitals; died Aug. 22, aged 68, of bronchopneumonia.

Weinstein, Max Irving ⊗ Methuen, Mass.; Middlesex College of Medicine and Surgery, Waltham, 1936; served during World War II; associated with Bon Secours Hospital in Methuen, Clover Hill Hospital in Lawrence and the Lawrence (Mass.) General Hospital where he died Aug. 15, aged 47, of coronary thrombosis.

Wood, William Ellege ⊗ Elgin, Texas; University of Georgia Medical Department, Augusta, 1902; died Aug. 1, aged 78, of heart disease.

Yadkowsky, Emanuel ⊗ Newark, N. J.; University and Bellevue Hospital Medical College, New York City, 1903; served on the staff of the Beth Israel Hospital, where he died Aug. 23, aged 74, of a heart attack.

Young, Harry Hopple, Robertsburg, W. Va.; Medical College of Ohio, Cincinnati, 1900; veteran of World War I; first director of the George Washington Life Insurance Company in Charleston; one of the founders of the original Charleston General Hospital; died in Charleston General Hospital Aug. 28, aged 80.

FOREIGN LETTERS

BRAZIL

Exfoliative Cytology of the Stomach.—Dr. Flavio San Juan compared the value of chymotrypsin lavage with the results of x-ray examination, gastroscopy, and estimation of gastric acidity in 82 patients (*O hospital* 53:513, 1958). The patients were divided into four groups: a control group of 20 with radiologically normal stomachs, 15 with peptic ulcers, 23 with benign nonulcerative lesions, and 24 with malignant neoplasms. In 77 patients (93.9%) the results of cytology were correct; in 3 (3.7%) they were inconclusive; and one patient gave a false-positive and another a false-negative result. The results of radiology were correct in 63 patients (76.8%), false-positive in 9 (11.0%), and inconclusive in 10 (12.2%). Gastroscopy, performed in 43 cases, gave correct results in 38 patients, or 88.4%. In the control group with normal stomachs the results of cytology, radiology, gastroscopy, and gastric acidity were always in complete agreement. In the group with benign gastric ulcers the results were correct in 100% of the cytological examinations, in 80% of the radiological examinations, and in 71.4% of the gastroscopies; but for the exact diagnosis, radiology had the first place, followed by gastroscopy. For the determination of the benign or malignant nature of the lesion, cytology was superior to other methods. Gastric acidity was the least valuable. Gastroscopy was the best method for diagnosing chronic gastitis in general, followed by cytology and gastric acidity as the best means of diagnosing extensive atrophic gastritis. Radiology was the best method for other types of benign lesions. In the investigation of the possibility of malignant transformation of benign lesions, cytology was the most accurate.

In the group with malignant neoplasms of the stomach, cytology gave correct information in 87.5%, followed by radiology (79.1%), and gastroscopy (76.9%). In this group cytology and radiology together gave the correct diagnosis in 91.7%, and when cytology, radiology, and gastroscopy were combined, a correct diagnosis resulted in 100%. In six patients in whom the diagnosis of cancer was made in an early stage, cytology gave correct information in all, radiology in 4, and gastroscopy, carried out in only three patients, gave one false-negative result. There was no correlation between the degree of malignancy and the cytological findings.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Broad-Spectrum Amebicide.—Amaral and Pires, (*O hospital* 54:75, 1958) treated a series of eight patients who were carriers of several species of intestinal amebas, including Entamoeba histolytica, with a new drug derived from phenantroline (preparation 11-925 C). After a seven-day treatment with 300 mg. taken three times a day, all amebas disappeared.

Hepatosplenomegaly in Children.—Dr. Denise Altenhein and co-workers of the São Paulo State University Hospital presented to the Associacão Paulista de Medicina a paper stressing the importance of the hepatosplenomegalic syndrome in children in diverse conditions with a certain pathogenic affinity. Icterus and anemia are frequent accompanying symptoms. In their series of 116 patients the abundance of signs, symptoms, and laboratory findings demonstrated the probable impossibility of making a diagnosis on the basis of hepatosplenomegaly alone, because such enlargements may be vascular, inflammatory, infiltrative, or tumoral. Anyway, it serves at least as a starting point for the diagnostic deductions. The patients were classified as having (1) diseases of the liver, including cirrhosis and malformations of the biliary ducts (32 patients); (2) diseases of the blood such as hemolytic anemias, leucemia, and reticuloendotheliosis (31 patients; (3) congenital syphilis (24 patients); (4) infections and parasitic infestations, including leishmaniasis and schistosomiasis (11 patients); and (5) vascular accidents such as thrombosis (4 patients). There were 14 cases of errors and omissions of diagnosis, including two patients with sympathoblastomas with metastasis in the liver.

FRANCE

Aortography.—P. Betoulières and co-workers (*Montpellier Médical*, vol. 52, no. 2, 1957) used a trocar with a short-bevel needle, a mandrel for obturation, and a sounding line fitting into a metallic conductor for aortography. As one passes the sounding line along the metallic guide in the trocar, an assistant injects a small quantity of a contrast medium to make sure of the exact location of the sounding line. The aortic tree may be made opaque by this method from the aortic arch to the iliac bifurcation. To visualize an arterial branch, bent sounding lines are used. The advantage of this method lies in the possibility of injecting the contrast medium at the de-

sired height and in the fact that a minimum of the medium is required. The technique presents no danger; it is safer than the usual method of aortic angiography.

Treatment of Drowning.—L. Fournier at the Concours Médical in March described a new treatment of drowning consisting of (1) parilaryngeal infiltration with a local anesthetic to stop spasm, (2) laryngeal intubation, and (3) precordial massage or intracardiac injection with epinephrine or arterenol.

Emergency Treatment of Corrosive Esophagitis.—Flottes and co-workers (*Annales d'oto-laryngologie*, March, 1958) treated a series of nine patients who had corrosive esophagitis with cortisone and ACTH. In each case a swallowed thread acted as a guide on which a sound could be passed. The thread was introduced through the nose and retained for at least one month or until cicatrization was complete. Thus alimentation was maintained without gastrostomy. This method permits the physician to follow the course of the cicatrization. Eight patients recovered without sequelae. The one failure was due to introducing the guiding thread too late.

Carcinogenesis.—In the *Bulletin de l'Association Française pour l'Etude du cancer* (vol. 44, no. 4) Lacassagne and co-workers reported a series of experiments comparing the cancerogenic action of cellophane, graphite, and mica. The authors found that sarcomas were produced in those rats in which a leaf of cellophane was wrapped around the kidney. In those with inclusions of mica and graphite no tumors developed, but a lamella of glass produced a fibrosarcoma.

Treponemic Antigens.—Vaisman and Hamelin (*Presse méd.* **66**:1397, 1958) stated that the serodiagnosis of syphilis has been facilitated by new methods making use of treponemic antigens in contrast with classic tests which use lipidic reagents. Hemolytic reactions with Ritter's treponemic antigen are more sensitive and more specific than those with the lipidic reagents but are difficult to perform. Hemolytic reactions with pathogenic Treponema pallidum as antigen (Portnoy's and Magnuson's antigen) gave results approximating those obtained from the Treponema immobilization test. The antigen is very stable. The adhesion-disappearance reaction consists in adhesion to human erythrocytes of the treponemas sensitized by the specific antibody in the presence of a complement. The test is difficult to evaluate. The Treponema immobilization test is already widely used. The authors concluded that it is the best because of its high specificity and great sensitivity.

INDIA

Coronary Disease.—A study of coronary heart disease by Malhotra and Pathania (*Brit. M. J.* **2**:528, 1958) does not support the commonly held view that it is less frequent in Eastern countries and that it is associated with a high fat intake. Data on 867 patients with coronary heart disease in the Punjab were collected from 3,054 patients with cardiac disease. Thus, coronary disease accounted for 28.4% of these. The maximum incidence of the disease was in the 50-to-59-year age group, which is a decade younger than the age group of maximum incidence in Western countries. In Western countries women suffer much less than men from coronary disease. The sex ratio in the literature varies from 1:4.2 to 1:6.6. In the Indian series the ratio was much the same, namely 1:6.7; yet in India women lead a comparatively sheltered and indoor type of life, and they are mostly vegetarians, nonsmokers, and teetotallers. The fat content of the diet taken by most of the Indian patients was low, compared with American and European standards; yet the incidence of coronary disease would appear to be of the same order. The authors found it difficult to believe that dietary fat could play any significant part in the causation of coronary disease. Their observations showed that vegetarians living on a low fat diet are no less likely to develop coronary disease than meat eaters. Tobacco did not appear to be a factor, as one half the patients were Sikhs, whose religion forbids smoking. They were no less susceptible to coronary disease than Hindus, whose religion does not proscribe it. Obesity has long been recognized as an associated factor in coronary disease. This was found to be so only in Indian women.

Patients were classified according to their socioeconomic status. The incidence of coronary disease was highest in the middle classes, intermediate in the upper, and least in the lower classes. As in Western countries those leading a "chairborne" life showed a higher incidence than those earning their living by hard physical work. The condition was far more common in the urban than in the rural population, but interpretation of the data obtained was difficult because the rural patient, unlike the town dweller, seeks medical advice only when he is severely disabled. A genetic factor plays a prominent part in the cause of coronary disease, according to the authors, who found a family history of ischemic heart disease in 33% of the patients. As in patients seen in the West, it was found that hypertension and diabetes were commonly associated with coronary disease.

Osteoarticular Lesions in Smallpox.—K. S. Bose (*J. Indian M. A.* **31**:4 [Aug. 16] 1958) stated that, although the incidence of osteoarticular lesions after smallpox is small, he observed 12 such cases

in one year; 9 of them occurred in the subacute stage of the smallpox attack two to six months after desquamation of scabs, and 3 occurred 1 to 12 years after the attack. Those observed in the subacute stage resembled pyogenic arthritis and osteomyelitis. Affection of the elbow and bilateral involvement were common features. One patient developed a sinus formation followed by bony ankylosis. The radiologic appearance resembled a chronic pyogenic osteomyelitis, but the ends of bones were also involved. Small cystic changes and subperiosteal bone formation without sequestrums or marked necrosis and new bone formation were characteristic. Both the epiphysis and metaphysis were involved along with joints. One patient, however, showed isolated bone involvement, while sequestrums and typical changes of osteomyelitis were seen in the patient who had developed a sinus. Joint changes consisted of erosion of articular ends, periarticular soft tissue swelling, and increase in joint spaces.

In two late cases, growth at the involved joint was interfered with, although movement was preserved to a great extent. In late cases in general the joint space was decreased with deformed articular ends and unequal growth causing valgus deformity. Microscopic examination of aspirated material and biopsy of synovial membrane, muscle, and capsule showed a few degenerated cells but no microorganisms. Culture of the aspirated material was also sterile. On microscopic examination, the bones showed changes resembling those of osteitis fibrosa. Pure bone lesions healed after curettage and scraping. Partial excision of the elbow joint was performed on two patients, one of whom did well. One patient who had developed genu valgum was subjected to a corrective osteotomy and obtained a good result. Sequestrectomy was performed on the patient with sinus formation. In five patients with comparatively early changes and swollen elbow joints, the joints were immobilized in plaster. A gradual improvement in movement of the joints with no recurrence was met with, although the movements of the elbow were not restored completely in any case.

Mental Deficiency.—Manchanda and Sagar (*Indian J. Child Health* 7:7 [July] 1958) reviewed 200 cases of mental deficiency in children and found that idiopathic mental deficiency accounted for 71.5%. About 50% of the rest gave a history of meningitis or encephalitis. Of the 200 children, 140 belonged to the poorer class; 77 came from rural areas, and the rest came from cities. The number belonging to the age group 0 to 1 was smallest, and about 67% were aged 2 to 5 years; 42.5% of the children were either first or second born and most of these were in the idiopathic group. Of the 69 mothers above 30 years of age, 26 were mothers of children with mongolism; thus 74.3% mothers of the 35 with mongolism were above 30 years of age. There were 184 children born full term, 15 were premature, and 1 was postmature. Thus prematurity was not a major factor in the causation of mental deficiency. A history of difficult labor was available in 44 cases, and 28 mothers had had some illness during the antenatal period, the commonest being fever of short duration. One had jaundice due to infectious hepatitis. One mother confessed attempted abortion. A family history of mental illness and epilepsy was obtained from only four patients, and none gave a history of consanguinity. Nineteen of the children had difficulty in breathing and cyanosis soon after birth; 11 of these had cerebral palsy, 6 had jaundice in the first week, and 6 had epileptiform fits in the neonatal period. Trauma, infection, and malnutrition occurred after birth in 31. The presence of mental deficiency was suspected by the parents of only 25% of the children below the age of 2 years. Most were brought to the doctor for some physical defect such as rickets, flat feet, or general debility. The idiopathic group included those with mongolism and microcephalics. This series did not contain a single case of congenital syphilis, although serologic tests for syphilis were made in all suspected cases. According to mental tests, 77 were idiots, 110 imbeciles, and 23 feeble minded; 107 were difficult and unmanageable.

Clinical Trials with Chloramphenicol.—S. M. Merchant (*Indian J. Child Health* 7:8 [Aug.] 1958) gave chloramphenicol monostearoylglycolate-3 to 77 children with various infections. The ester was found to give the same blood level as that obtained by administration of free chloramphenicol in animal experiments and in tests on human beings. The series included 29 patients with whooping cough, 21 with enteric infection, 16 with bacillary dysentery, and 11 with neonatal infection. Twenty-one of the 29 with whooping cough obtained excellent results, but in 3 there was no improvement; 4 developed mild diarrhea which did not call for withdrawal of the drug. All but two of those with enteric infection did well, the temperature returning to normal within 72 hours; four developed slight diarrhea. All of those with bacillary dysentery responded well, both the fever and diarrhea being controlled within 24 hours. Eleven neonatal patients with undiagnosed infection responded well.

Neomycin-Sulfadimidin for Infant Diarrhea.—Gupta and Pohowally (*Indian J. Child Health* 7:8 [Aug. 18] 1958) treated 40 unselected children under the age of 2 years for diarrhea with a suspension containing neomycin, sulfadimidin, pectin, and kaolin, and the results were compared with those obtained in a control group of 60 children also under 2 years of age who received sulfadiazine, chloramphenicol, or

streptomycin, singly or in combination. Patients were considered cured when the number of stools was less than five in 24 hours, consistency was solid or semisolid, no blood or mucus was seen on macroscopic examination of stools, and microscopically there was no blood or mucus and less than two pus cells per high-power field. There was no difference in the incidence of diarrhea in breast fed infants and those reared on mixed or artificial feeding. In each group 55% obtained a five-day cure. Stool culture showed a predominance of Escherichia coli, and these patients responded well to the neomycin-sulfadimidin therapy. This combination, however, did not seem to have any advantage over the standard therapy for diarrhea.

Liver Function Tests.—K. H. Nair and co-workers (*J. A. Physicians of India* 6:3 [July] 1958) studied 52 patients with cirrhosis of the liver, congestive splenomegaly, hepatitis, and carcinoma of the liver in persons above the age of 12 years. The maximum age incidence was between 20 and 40 years. About 44 complained of anorexia and pain in the abdomen. Ascites was present in 29. The enlargement of liver varied from just palpable to five fingerbreadths below the costal margin. The spleen was also enlarged in about 10, and it was noticed that in all patients with associated splenomegaly, ascites was present. There was no relation between the size of the liver and the presence of ascites. The thymol turbidity test varied from 2 to 10 units and was not related to the degree of enlargement of the liver and presence or absence of ascites. In patients with a raised icterus index and a direct immediate Van den Bergh's reaction, it was above 7 units. The serum protein level varied from 6.0 to 10.2 Gm. per 100 ml., and variation in total protein levels were not related to the thymol turbidity test, Van den Bergh's reaction, and icterus index. The total serum protein levels were lowered in only three patients, but there was a change in the normal albumin-globulin ratio, the latter being raised. This ratio was not normal in any patient and varied from 1:1 to 1:3. The alkaline phosphatase estimation gave normal values, while the protein content of the ascitic fluid was found to be below 1.5 Gm. per 100 ml. The Kahn reaction was positive in 12 patients. The authors suggested that in addition to protein deficiency, exposure to infection and the stress and strain of life are probable etiological factors. Most of the patients with a high serum protein level and a diminished albumin-globulin ratio were highly toxic and even cholemic, the degree of cholemia being related to the increase in globulin. The case fatality rate was also higher in patients with a high globulin level.

Complications of Measles.—Silhar and Maru (*Indian J. Child Health* 7:7 [July] 1958) reported a series of 315 patients who had measles with complications. The maximum age incidence was seen in children between 1 and 2 years old, the youngest patient in the series being 4 months old; 80% were under 4. In this series 50% had respiratory complications; 30% had alimentary complications; and 6% had central nervous system complications. Otitis media, supposed to be a common complication of measles, was comparatively rare (less than 3%). Respiratory complications included bronchitis, bronchiolitis, bronchopneumonia, upper respiratory tract infection, and reactivation of pulmonary tuberculosis. Most of these occurred within the first 10 days of appearance of the rash. All the patients with bronchiolitis were under 18 months of age. While a combination of penicillin and streptomycin was found useful in the treatment of these complications, adequate doses of sulfonamides given in time were also effective. The main alimentary complications were enteritis, gastroenteritis, and dysentery. Stool examination was uniformly negative. Sulfadiazine, streptomycin, and chloramphenicol were useful in the treatment of these complications. The central nervous system complications included 14 patients with encephalitis, 3 with tuberculous meningitis, and 1 with a flare-up of febrile convulsions; 11 cases of encephalitis occurred within two weeks of appearance of the rash, 1 after three weeks of appearance of the rash, while in 2 it preceded the appearance of the rash. Other complications included skin infection in 10 and eye and ear infection in 10. As sequelas of measles, anemia developed in 14 patients and malnutrition in 8. The largest number of patients in this series came from treatment in the second week; 90% had had no treatment in the preeruptive or eruptive phase. There were three deaths, all occurring within 48 hours of hospitalization, two patients dying of encephalitis and one of tuberculous meningitis.

Effect of Soluseptasine on Blood Sugar.—Bhattacharya and Goswami (*Antiseptic* 55:7 [July] 1958) studied the effect of intravenous injections of Soluseptasine (a sulfonamide) on the blood sugar level of 50 men in hospital. Patients with liver, kidney, and heart diseases were excluded. A preliminary glucose tolerance test was done in all patients, four days later fasting blood samples were taken, and then 5 cc. of 20% Soluseptasine was given intravenously; 50 Gm. of glucose was given orally after the injection, and blood samples were collected every half hour for two and one-half hours and after three and one-half hours. Urine was also collected at half-hourly intervals and examined for sugar. Some urine samples in 13 patients showed sugar. The blood-sugar lowering effect of Soluseptasine was evident in 30 minutes and reached its maximum in one and one-half to two and one-half hours. Four patients showed signs of hypoglycemia, and two had only glycosuria. The authors suggested

that a liberal supply of carbohydrates should be given to patients who are receiving sulfonamides intravenously.

Sanitary Engineering.—The government agreed to the payment of stipends, fees, and other expenses to sanitary engineers and auxiliary sanitary engineering personnel for training in the implementation of a national water supply and plans for sanitation. In the year 1958-1959 such stipends will be given to 45 trainees for training as engineers for a period of 10 months. Those taking the course will be eligible for the stipends from the date they join the course. Another group of 150 engineers will get stipends for a three-year course at the All-India Institute of Hygiene and Public Health, Calcutta, and the Engineering Colleges at Roorkee and Guindy, where stipends will also be given to 180 engineering subordinates for a three-year course. Other personnel who will be receiving assistance include 100 waterworks operators and 50 sanitary inspectors to be given short courses at various regional centers.

Tuberculosis.—In an address before the Tuberculosis Association of Madras in July, the minister of health said that about 500,000 persons died every year of tuberculosis and 2,500,000 were suffering from it at any given time in this country. The health panel of the planning commission had estimated that the needs of the country in this field at the start of the first five-year plan were 4,000 tuberculosis clinics, 500,000 beds, 15,000 physicians, 50,000 nurses, and 12,000 home visitors. The gap between the needs and the available resources could be seen from the fact that there were only 160 tuberculosis clinics and 7,000 hospital beds at the beginning of their planning. While it was necessary to increase these facilities, most of the emphasis must be on prevention rather than cure, on domiciliary services rather than hospital care, and on early diagnosis rather than on surgery. The transmission of the infection must be prevented through isolation at home as well as hospital treatment. There is a great need for voluntary assistance in this sphere. The Tuberculosis Association of India, a voluntary organization, has done a great service in this connection. Public interest has been awakened to the importance of the problem.

Epidemic Encephalitis.—In Nagpur, with a population of 500,000, between June 26 and July 4 there were 20 children between 1 and 10 years of age admitted to hospital (*Indian Journal of Child Health*, Aug., 1958). All 20 died. Some gave a history of acute diarrhea, vomiting, dehydration, and convulsions; others had hyperpyrexia, vomiting, and convulsions. Death occurred within 24 hours of admission. Children with this disease admitted between July 4 and 8 were not as sick, and some survived. All of those admitted after July 8 survived. The admission rate then declined rapidly. Similar cases were also seen in private practice, but their mortality was low, one death being reported in 24 cases. Physicians reported having seen such patients almost every year at this season, although their number was smaller and the treatment was mostly symptomatic. At the hospital, these children received chloramphenicol routinely, and those that survived could be discharged on the third day. The only neurological sign in these patients was muscular rigidity of the neck and back. The spinal fluid showed no definite abnormality, and blood, stool, and urine specimens and throat swabs revealed no causal organism on culture. The cause could be a virus. No residual paralysis or any other neurological sign was seen in the survivors.

UNITED KINGDOM

Triamcinolone.—A clinical trial with a new Δ^1 cortisone analog containing fluorine (triamcinolone) was made by Hart and coworkers (*Lancet* 2:495, 1958) in 30 patients with rheumatoid arthritis, systemic lupus erythematosus, and ulcerative colitis to compare it with prednisolone and ascertain its side-effects, particularly those affecting the stomach. The dose of the drug was four-fifths that of the prednisolone given previously. All the patients with rheumatoid arthritis kept daily records of pain, stiffness, the number of analgesic tablets needed daily, and the time it took to loosen up in the morning on rising. Observations were also made every three or four days of joint tenderness in the fingers, finger swelling, and strength of grip. The sedimentation rate was determined weekly. Of the 25 patients with rheumatoid arthritis 11 improved, but in only 5 was improvement more than slight; 11 preferred triamcinolone to prednisolone. Of seven patients who complained of dyspepsia while taking prednisolone, three improved when they changed to triamcinolone and three were made worse by the change. The condition of the patients with lupus erythematosus and ulcerative colitis was unchanged after being given triamcinolone.

The authors concluded that triamcinolone is another effective steroid with no particular therapeutic virtue, except that it does not cause salt and water retention. One of the side-effects noted was postprandial flushing. Wells gave the drug to 14 patients, previously maintained on therapy with prednisolone, for various conditions (*Lancet* 2:498, 1958). Of nine with no previous history of joint symptoms, three developed arthritis, which in two resembled acute rheumatoid arthritis. He suggested that the change of therapy from one steroid to another was responsible. Apart from this episode, he considered the therapeutic effectiveness of triamcinolone to be superior to that of prednisolone.

CORRESPONDENCE

TOXICITY AND ANTIPYRETIC ACTIVITY OF SALICYLAMIDE AND ASPIRIN

To the Editor:—In THE JOURNAL of Aug. 9, 1958, page 1821, the article "Antipyretic Effectiveness of Salicylamide and Acetylsalicylic Acid in Infants" by Vignec and Gasparik contains a number of misleading statements. These become even more disturbing after the reading of their references and the pertinent literature.

The authors say: "Actually, if one can extrapolate from the observed LD_{50} for mice . . . it is difficult to see how a child might ingest dangerous amounts [of salicylamide]." This extrapolation is then accepted as a scientific fact, because in their conclusions they state that "the greater margin of safety of salicylamide must also be taken into account." The authors refer to Seeburg and others (*J. Pharmacol. & Exper. Therap.* **101**:275-282 [March] 1951) as their basis for stating that the LD_{50} of salicylamide is "approximately twice that of aspirin." Actually, Seeburg presents no data on LD_{50} in this article.

TABLE 1.—*LD_{50} Values in Mice, in Grams per Kilogram of Body Weight, After Ingestion of Salicylamide and Aspirin*

	Salicylamide (SAM)	Aspirin (ASA)	Ratio SAM:ASA
Drebinger (Medizinische 7:795-797 [June 7] 1952)	1.14	1.87	0.61
Curron and others (Therapie 7:27-36, 1952)	0.60	0.83	0.75
Hart (J. Pharmacol. & Exper. Therap. **99**:295-309 [March] 1947)	1.40	1.10	1.27
Bavin and others (J. Pharm. & Pharmacol. **4**:872-878 [Nov.] 1952)	1.59	1.30	1.22
Boxill and others (J. Am. Pharm. A. Scient. Ed. **47**:479-487 [July] 1958			
Fasting	1.20	0.96	1.26
Nonfasting	1.50	1.00	1.50
Matsumura (Fol. Pharmakol. Japan **50**:99, 1954 [From Bekemeier, Arzneimittel-Forsch. **5**:572-575 (Oct.) 1955])	1.15	0.75	1.53

A search of the literature discloses six reports (table 1) on the oral LD_{50} values in mice in grams per kilogram of body weight. Two of the reports show salicylamide as the more toxic, and four show aspirin as the more toxic. However, in no case is aspirin reported to be twice as toxic.

Justification for the statement that aspirin is approximately twice as toxic as salicylamide has not been found, even when a thorough search of the literature was made for all species. Oral LD_{50} values reported for the rat, rabbit, guinea pig, and cat in grams per kilogram are shown in table 2.

It can be seen from these values that the relative toxicity of salicylamide and aspirin administered orally varies in the same species under different conditions and in different species. In rats, two authors found salicylamide to be more toxic and two others found aspirin the more toxic. Oral LD_{50} values in cats show that salicylamide is approximately three times as toxic as aspirin; while on the other extreme in the rabbit salicylamide is reported as approximately 0.6 as toxic as aspirin. It is difficult to see how any extrapolations from these reported values in animals could provide a valid relative toxicity ratio for humans that would show one drug to be less toxic than the other.

TABLE 2.—*LD_{50} Values, per Kilogram of Body Weight, in Experimental Animals*

	Species	Salicylamide (SAM)	Aspirin (ASA)	Ratio, SAM:ASA
Hart (J. Pharmacol. & Exper. Therap. **99**:295 [March] 1947)	Rat	1.40	1.50	0.93
Boxill and others (J. Am. Pharm. A. Scient. Ed. **47**:479-487 [July] 1958)	Rat	0.98	1.43	0.68
Drebinger (Medizinische 7:795-797 [June 7] 1952)	Rat	1.49	1.24	1.20
Ichniowski and Heuper (J. Am. Pharm. A. Scient. Ed. **35**:225-230 [Aug.] 1946)	Rat	>2.00 2.00	>2.00 1.00	1.00 2.00
Boxill and others (J. Am. Pharm. A Scient. Ed. **47**: 479-487 [July] 1958)	Guinea pig	1.73	1.07	1.60
Hart (J. Pharmacol. & Exper. Therap. **99**:295-309 [March] 1947)	Rabbit	>3.00	1.80	>1.60
Bekemeier (Arzneimittel-Forsch. **5**:572-575 [Oct.] 1955)	Cat	0.1-0.15	0.409	<0.25 to 0.37

* The widely different results reported require clarification.
† Value of 0.4 is for salicylic acid which is more toxic than aspirin.

The statement of Vignec and Gasparik, in their summary and conclusions, that "a comparative study of the effectiveness of salicylamide (Liquiprin) and acetylsalicylic acid (aspirin) indicated that both drugs controlled pyrexia . . . equally well and with the same number of doses," is extremely misleading. Though approximately the same number of doses were required, each dose of salicylamide was twice that of aspirin. Therefore, twice as much salicylamide was administered over the same period of time. With evidence that salicylamide and aspirin are each more toxic than the other under certain conditions and in certain species, the use of twice the dose of salicylamide in their study would appear to be the more hazardous procedure. Actually, the doses of salicylamide used in their study were two to three times the recommended doses as stated on the label and package (table 3). No explanation was given for the use of these larger doses.

TABLE 3.—*Doses as Used by Vignec and Gasparik and as Recommended by Manufacturer*

Age	Dose, Mg. Used	Dose, Mg. Recommended	Ratio, Dose Used: Dose Recommended
0-6 mo.	64	30	2.2
6-12 mo.	178	60	2.1
1-2 yr.	256	130	2.1
2-3 yr.	384	200	1.9

It is well known that the temperature of children is quite labile and that fever "breaks" and disappears spontaneously in many instances. The absence of any control untreated children in the study is indeed unfortunate. The many items cited above justify withholding judgment on the comparative toxicity and antipyretic activity of aspirin and salicylamide until adequately controlled studies are available.

ROBERT A. WOODBURY, M.D.
University of Tennessee
Memphis 3, Tenn.

PATHOLOGIST'S DEATH CERTIFICATE

To the Editor:—An interesting and timely article, "What Is 'the Cause of Death'?" by Erhardt, appeared in THE JOURNAL (168:161-168 [Sept. 13] 1958). The author is primarily making a plea for accurate death certificates so that they can have valid meaning in compiling scientific, medical, and public health reports. He states, "Solely the physician in attendance, therefore, can judge adequately which of several conditions was the most important factor in the death of the patient."

As a pathologist, I wish to challenge the validity of this statement and to offer some constructive suggestions. Many people die without benefit of medical attendance except terminally, especially when death is sudden, as it often is. Many people change physicians for their terminal illness, calling in the nearest physician or the first physician they succeed in contacting. Many patients are transferred from the neighborhood physician to a strange physician in a nearby hospital for their terminal illness. Many people die and are certified by coroners who are sometimes laymen and often without benefit of autopsy. People move to new communities and have new doctors. It is said that one-fifth of the population of the United States moves to a new home each year.

Even when people die in hospitals and have been fully and adequately studied, the cause of death, as certified, is incorrect in a high percentage of cases when there is no autopsy. The accuracy of "the cause of death" as determined by clinical findings alone is probably no greater than 40%, a charitable estimate. There are many possible discontinuities in the clinical study of a patient which cannot always be avoided.

The point is that death certificates are not very accurate and cannot be expected to be very accurate even under the highest standards of present-day clinical practice. I have known of instances where the physician did not know the cause of death and freely admitted this. Coroners usually refuse autopsies on this ground alone and inform the physician to make the best guess he can, which usually turns out to be "heart failure."

There is only one effective way to make death statistics accurate and that is to base them, where possible, on the findings of autopsies performed by competent pathologists. The large mass of accurate autopsy data which is accumulated in hospitals today is mostly wasted as far as death statistics are concerned.

Question No. 20 on the standard death certificate —Autopsy? Yes, No—is of little help. The inference is that if there was an autopsy, the death certificate was completed on the basis of the autopsy findings. This is not necessarily so. The physician is not required to use the autopsy findings and frequently does not do so. The death certificate is sometimes completed when the person is pronounced dead, without waiting for autopsy findings and without knowing whether there will be an autopsy. In some places, this is standard practice and is encouraged or enforced by administrative rule. In addition, "the death certificate cannot wait." It must be completed promptly for the convenience of the funeral director and the survivors so that prompt funeral arrangements and burial can be made. It may take several days or even weeks to complete the scientific autopsy studies.

If the states, the public health people, and the vital statistics workers want accurate death statistics they can have them and they can have them in abundance. Supplemental death certificates, which might be called "Pathologist's Death Certificates" should be legally authorized. Pathologists should be required to complete such certificates for all autopsies that they perform and submit them to the vital statistics officer concerned within a reasonably limited period of time, such as 60 or 90 days.

A legislative program such as this would produce a large volume of highly accurate data on the causes of death and should, in the long run, result in many scientific medical advances. At least, we would have an accurate scientific picture of what the most important medical problems are. Autopsies do not always disclose the true cause of death, but their accuracy, when they are properly performed, is about 98 to 99%.

Today, the pathologist completes his scientific labors in his rather highly accurate field of work, writes his report, and finds it buried in the hospital record room, just as effectively buried as the body on which he performed the autopsy. A small percentage of these reports are used locally for teaching purposes. A still smaller percentage, usually the rarest cases, are published.

The supplemental death certificate is not without precedent. They are used in a limited way in a few jurisdictions. It is my understanding that the city and county of San Francisco started using such certificates on an optional basis many years ago. There should be a separate and mandatory "Path-

ologist's Death Certificate" in all cases of autopsy. Such a death certificate might occasionally cause embarrassment to a few physicians. It should be no greater than that which tissue committees now cause occasionally in the case of surgeons. Any small individual embarrassment would be a small price to pay where the greater public welfare is at stake. When the realities of the matter are studied, there should be no embarrassment at all for any physician. In the present state of development and utilization of medical science, no physician should be expected to have an omnipotent ability to determine "the cause of death."

EDWIN E. ZIEGLER, M.D.
West Kay Drive
Haddonfield, N. J.

THE LEISURE CORNER

GEMS AND PRECIOUS STONES

During periods of peace and prosperity gems and precious stones have many purchasers. All minerals and stones that are used for jewelry and other ornamental purposes are called gems. During war and depression the more valuable gems are sold, traveling from one owner to another and from one country to another. Historically speaking, there seems to be an interrelation between war and jewelry. Centuries ago warriors frequently carried their jewels with them into the thick of battle. Not too long ago the royal sale of jewels and precious stones provided funds for the conduct of war, while private individuals sold their gems so that they might survive. It still works both ways today—for martial governments on the march and for ordinary mortals. Heirlooms cherished for generations by families often find methods and means for entering exclusive shops on Fifth Avenue—the purpose, of course, to be sold. War has a characteristic way of poking greedy fingers into jewel boxes and then tossing the loot where it may.

Hardness, color, brilliance, rarity, and demand determine the value of gems. As a rule, diamonds are prized gems because they surpass all others in hardness and brilliance. Probably the most famous and celebrated diamond in the world is the Kohinoor, which was presented to Queen Victoria, in 1850, by the East India Company. The Cullinan diamond was famous because it was the world's largest at one time, weighing a little over 1.5 lb. before it was cut into 2 large stones, 7 smaller ones, and 96 others of lesser size. The largest of these, the 530-carat Star of Africa, is among the crown jewels of England and is set in the royal scepter.

A diamond of the highest degree of purity and fineness is said to be "of the first water." Color is the most important factor in judging a diamond. Those of the finest quality are perfectly clear. Some varieties of diamonds are green, orange, red, yellow, or blue. The most valuable ones are those in which the tint is decided and equal throughout. Even the lightest tint of a different color in a diamond affects its commercial value unfavorably and the finest gems can be spoiled by poor cutting. Rubies are more valuable than sapphires because they are rarer, although both have the same degree of hardness. The value of sapphires depends on the quality of their blue color. The emerald is often as valuable as the diamond, and its value is determined by size, freedom from flaws, and the shade of the green color. Pearls are graded by size, color, and perfection of shape, while opals are valued according to their color flashes. The so-called black opals are the most valuable.

In general, experts identify different kinds of gem minerals by the shape of the uncut crystals, color, index of refraction, hardness, specific gravity, and other properties. The shape of crystals differs with each gem material, but the shape of all crystals in any one mineral is usually the same. Color is one of the major factors in determining the beauty and splendor of gems. There are two types of colors in gems, essential and nonessential. Essential color is the color of the mineral itself, when pure, while nonessential color is the result of an impurity in the mineral. Minerals with a low index of refraction (the measurement of the speed of rays of light passing through a mineral) usually display a low luster. Hardness is an important quality of gem minerals. Few stones can become valuable gems unless they will wear for a long time. A scale has been established to indicate the sequence of hardness of each gem material, and it numbers from 1 to 10. Only minerals with a rating of seven or more wear well as gems. The diamond is the hardest and has a rating of 10.

The underlying rock type is the prime factor largely determining the kind of gem minerals found all over the world. Turquoise is found in great quantities in the southwestern part of the United States as well as in Tibet. Opal and turquoise are found where there is little rainfall. Emerald, topaz, and tourmaline are found in areas where erosion has exposed old, once molten rocks at the surface. Emeralds are found in the Ural Mountains, Colombia, and South Africa, while the finest topaz comes from Brazil. The best rubies come from Burma and the best sapphires from Kashmir. The finest opals come from Australia, and the most desirable pearls are derived from the waters of the Persian Gulf and the South Pacific Islands.

The beauty of a gem stone depends largely on its luster; hence, the appearance of a gem is somewhat equivalent to the texture of a flower. As a matter of fact, the word gem comes from the Latin word gemma meaning bud, and the story of precious stones can be compared to the blooming of flowers. An authority on gems recognizes the following eight different types of luster: (1) adamantine: a luster characteristic of diamonds; (2) vitreous: having an appearance of broken glass (as sapphire, ruby, topaz, tourmaline, and rock crystal, which are all transparent, vitreous in luster); (3) metallic (only opaque gem stones, for example, hemetyte and pyrite); (4) pearly: like a pearl (as moonstone and opal); (5) waxy (as turquoise); (6) resinous (as garnets); (7) silky (as green malachite); and (8) oily (as chrysolite).

The craftsman—sometimes a painstaking hobbyist—who cuts, polishes, and engraves gems is known as a lapidary. The word itself is derived from the Latin word lapis, meaning stone. Lapidaries flourished in Assyria and Babylonia several thousands of years ago. A sapphire point was used in cutting until about 3,000 B. C., when the bow drill was introduced. Contemporary gem cutters employ a lathe with a point or disk of soft iron, coated with diamond dust and oil. Before the 1300's most gems were polished smooth and closely retained the original size and color of the stone. The practice of cutting flat surfaces or facets is fairly modern.

Since nature yields her precious stones reluctantly and only the comparatively well-to-do may own them, the craving for gems has gone on for centuries. This, in part, has been satisfied by the glassmaker, the alchemist, and the chemist. Imitation gems have a wide market. Today, the basis of most imitation gems is a soft glass called paste or strass. This glass is clear and brilliant, and is made of pure powdered rock crystal, red lead, and dry potassium carbonate. Imitation gems made from this paste can be scratched easily. White sapphires, colorless zircons, and clear quartz make inexpensive substitutes for diamonds. An old-time formula for making a sapphire reads as follows: "Take a crystal, 1 lib., grind it very fine and sift it, afterward put ½ lb. of the powder of stags bones burnt, if you can procure them, if not of other animals, or sal. alkali lib. ½, grind all very fine, and mix them well together. Take this powder and put it into a strong pot, covered and luted outside; when you have cooked this in a glassmakers' furnace, allow it to remain for 5 or 7 days, and it is there melted like glass. Afterwards place good 'azurio ultramarino' (made from lapis lazuli) and being mixed together will make the beautiful blue tone for making sapphires." Certainly, the old-timers had a formula for it.

Today, the chemist does not go in for hunting a stag and burning its bones to assist him in creating artificial gems. In recent years, synthetic gems of good quality have been produced in the laboratory. Rubies and sapphires have been made with chemical and physical properties that simulate the original. Nonetheless, the artificial gem cannot qualify as a true gem. Nothing can take the place of a mineral that nature has formed, unassisted by chemists. The dominant qualities that stand out in a true gem include outstanding beauty, sufficient hardness to retain that beauty, and the rarity that only the wonders of nature can produce.

BUSINESS PRACTICE

This is the fourth in a series of excerpts from the brochure on the Business Side of Medical Practice, prepared by the American Medical Association in cooperation with the Sears-Roebuck Foundation.

LOCATING THE OFFICE

The next action a doctor must take who has selected his community and checked into licensing questions is to find an office. He has to decide whether to build, remodel, or rent space.

Building an Office

Although the idea of planning the ideal medical office from the ground up is appealing, few doctors starting out in practice have enough money to do so. Some doctors think it is wiser to practice in a community and definitely determine practice needs before building. Too often a doctor who has hurried into building programs discovers later that the office meets neither his nor his patients' needs.

For the physician who can build his own office there are some words of advice: 1. Consider the most ideal location from your standpoint as well as the patients' standpoint. 2. Check with a reliable realtor about property availability. 3. If the building site is in a residential zone, check with the zoning commission to find out if medical offices are allowed. 4. Make sure the sewer, water supply, electric service, telephone service, and gas service are adequate. This is particularly vital in suburban areas. 5. Get the consulting services of an architect to help make the final decision about purchase of the property. Utilize his services in design of the proposed building. (In most communities services of a member of the American Institute of Architects can be secured.) 6. Building an office is a business venture, involving expenditure of considerable cash. The whole process should be conducted in a business-like manner with the aid of experts secured to make sure it is a sound investment.

Renting an Office

The doctor who decides to rent is sometimes limited in the selection of a location by what space is available. In the suburbs and smaller towns ade-

quate office space may be hard to find. He probably will be offered these possibilities: space in a downtown medical center or office building, a suburban location, or a combination home-and-office arrangement (see table).

It is best to analyze all the possibilities in terms of the kind of practice envisioned and the doctor's own personal desires.

Office Essentials

In deciding on an office location, there are several factors which should serve as a yardstick. Is it accessible and convenient from the patients' standpoint? Obviously, if it is six blocks from the end of the bus line or if patients have to run outside to deposit pennies in a parking meter every few minutes its location leaves something to be desired. Is it adequate space-wise and convenient from the doctor's standpoint? The beginning doctor generally can manage with a reception room, examining room, and consulting room for the first year, but he soon will need more room. If the layout of the office is inconvenient for the physician, he'll waste valuable minutes and tire himself out working in it. It probably is wiser to take a long-range approach to selection of an office location and pay rent on an extra room or two at the outset rather than try to secure more space later or move to a new location.

The less remodeling required, the better. However, remodeling is sometimes a quick, easy, and fairly inexpensive way to establish a new medical office unit. Store buildings and large residences often can be converted into medical offices with a fairly small original investment. The feasibility of remodeling should be determined only after consulting experts—builders and architects who can appraise the structure, the adequacy of heating, plumbing, electrical systems, and the possibilities for efficient office layout.

A physician who remodels or makes minor alterations in leased or rented space should protect himself with a long-term lease, since all the money he invests is the landlord's gain. If the landlord pays for improvements, the cost shows up in higher rents. If the tenant pays, he can amortize the investment over the period of the lease for tax purposes.

Office Planning Guide

A detailed planning guide for establishing medical practice units, complete with checklists for evaluating possible office locations, plans for various types of offices, and lists of necessary equipment, is available to physicians on loan from the American Medical Association's Council on Medical Service. The U. S. Public Health Service also has available an office planning guide for physicians.

Plan carefully when setting up an office. The kind of practice and the speed with which it is built depend to a large extent upon the location and arrangement of the office.

Leases

"Look before you lease" is good advice for any tenant. It pays the physician to go over a lease line by line, preferably with an attorney, so that he knows exactly what he is signing.

Every lease should contain a description of the premises, including rooms and other storage space, and list any furnishings to be provided with a description of their condition. It should stipulate what services are to be furnished by the landlord in the way of utilities, janitor, and elevator service (if any) and who pays for decorating, alterations, and the expense of restoring the premises to their original condition when the doctor moves out.

Pros and Cons of Office Locations

Pro	Con
Downtown Medical Center	
Space designed for M.D.'s usually available	May be costly, cramped
Other M.D.'s available for referral; good for specialists	Patients may not be able to find a doctor marooned in a downtown "ivory tower"
Auxiliary medical services available nearby	Parking space may be difficult to obtain
Neighborhood or Suburban	
Good for GP's, internists who draw patients from the area; more specialists also settling here	Space may be at a premium or available offices may need extensive remodeling
Space for parking usually available	May not be near public transportation; not all families have two cars
May not be many other doctors in the area	Neighborhood may appear to be good but beginning downhill slump
Office can be more home-like, informal	May have to settle for upstairs office which is not ideal for patients
Home and Office Combination	
Saves time and money	Seldom satisfactory, not enough privacy for patients, and doctor never escapes from practice; check zoning

Provisions should be included for subletting part or all of the premises in the event that the physician is unable to continue as a tenant. The doctor should also be relieved of any further liability should another tenant be assigned the lease. A right to terminate the lease is also advisable should a physician find it necessary to move for professional or other reasons.

An option to renew, specifying that the notice to renew the lease must be in writing, and submitted on or before a certain date, is a definite advantage to the doctor. Another possibility to consider is this: in leases covering more than three years it sometimes can be arranged that the monthly rental to a doctor just setting up practice is lower during the first year with the difference made up by higher monthly rentals later. Sometimes a landlord, anxious to secure a doctor-tenant, will provide a month or two of free rent. All possibilities should be investigated before signing, and any verbal promises should be put on paper.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Aplastic Anemia: An Analysis of 50 Cases. D. N. Mohler and B. S. Leavell. Ann. Int. Med. **49**:326-362 (Aug.) 1958 [Lancaster, Pa.].

The authors studied 50 patients with aplastic anemia, their ages ranging from 4 to 82 years, at the University of Virginia Hospital in Charlottesville between 1933 and 1956. All the living patients have been followed for at least a year, and only 2 have been lost to follow-up. The other 35 were followed until the time of death, and autopsies were performed on 14. The peripheral blood and bone marrow of each patient were examined, and in each instance there was evidence of defective blood production. Patients were excluded from this study if they had chronic infection, malignancy, malnutrition, renal disease, or liver disease, conditions known to depress bone marrow functions, or if they had been treated with agents such as nitrogen mustard derivatives, urethane, and irradiation. Patients with myelofibrosis and myeloid metaplasia were also excluded. The most common symptom was weakness associated with a bleeding tendency, such as epistaxis, menorrhagia, and bleeding from the gums. All the patients with hemorrhagic manifestations had thrombocytopenia, but not all the patients with thrombocytopenia had abnormal bleeding. Most of the patients had pancytopenia, macrocytic anemia, relative lymphocytosis, and hypocellular bone marrow. However, in 13 patients the bone marrow was normocellular or hypercellular, and 7 patients had anemia that was not associated with leukopenia or thrombocytopenia. Although the most important factor in the anemia in these patients was deficient erythrocyte production, the presence of an associated hemolytic component, manifested by increased fecal urobilinogen excretion and mild reticulocytosis, was not unusual. Exogenous hemochromatosis was found in 6 of the 14 patients on whom autopsies were conducted. Brownish-gray skin pigmentation, lymphadenopathy, hepatomegaly, and splenomegaly occurred commonly in patients who received multiple transfusions. Toxic exposure was thought to be the etiological agent in 7 patients, while the cause was unknown in 43.

The prognosis was most favorable in patients with anemia alone and in those with hypercellular bone marrow. However, an illness of long duration was not uncommon in those with pancytopenia and hypocellular bone marrow. Although 12 of the 37 patients who presented with pancytopenia died within a year, 6 lived more than 5 years and 1 survived 20 years. A complete remission occurred in 6 patients, and a partial or temporary remission in another 6 patients. Both the spontaneous remissions and those that followed corticosteroid therapy and splenectomy occurred most often in patients who had anemia alone.

New Results in Treatment of Acute Leukemia with Metacortandracin. R. Picard, J. Horeau, J. Guillon and C. Robin. Presse méd. **66**:1064-1067 (June 14) 1958 (In French) [Paris].

The authors present a follow-up of 6 patients with acute leukemia, whose cases were previously reported (*Presse méd.* **64**:301-302 [Feb. 18] 1956, an abstract of which was published in THE JOURNAL **161**:648 [June 16] 1956), and the results obtained in 19 additional patients, all of whom were treated with prednisone (Metacortandracin). The incidence of this disease in subjects less than 40 years was 70%; 18 patients died after periods of illness ranging from 4 days to 13 months. The average survival time was somewhat more than 4 months. The deceased patients were classified in 3 groups according to the duration of the disease; 5 with acute forms, who had a survival time of less than 1 month; 10 with subacute forms, who had a survival time of 1 to 6 months; and 3 with prolonged forms, who had a survival time of about 1 year. Two patients were lost to follow-up, and 5 patients are still alive. Of 2 surviving patients who have had remissions lasting several months, 1 is still alive after a follow-up of 20 months, and the other after 17 months. The other 3 living patients have had a follow-up of about 10 months.

The prednisone therapy was started with a standard dose of 100 mg. (larger doses of 250 or 500 mg. did not seem to be more effective), which was administered for 3 or 4 days and then gradually decreased by 10 mg. at a time until a maintenance level was reached in about 2 weeks. The mainte-

The place of publication of the periodicals appears in brackets preceding each abstract.

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nance dose was just enough to prevent reappearance of signs of the disease. This dose may be given, in principle, for an unlimited time. Prolonged treatments, lasting from 1 to 10 months, have been carried out by the authors in 12 patients. The current total doses in this series were of the order of from 5 to 7,000 mg. of prednisone. A record high of 12,000 mg. was given to 1 patient. Treatment had to be interrupted in only 2 patients.

The initial dose of prednisone was evidently of the greatest importance in regard to the restoration of a normal body temperature. It also had a good effect on the general well-being of the patients, except in those who died within a few days. Failure to obtain a good effect on the temperature by the treatment indicates a rapidly fatal outcome of the disease. Treatment with this drug, however, is not only ineffective but may even be dangerous in patients with fever of infectious origin; consequently, a careful and thorough search for a focal infection should be made, and in doubtful cases the systematic administration of antibiotics is advisable. Beneficial effects of the administration of prednisone on osteoarticular pain have been observed, except in a few patients with localized foci which, on the contrary, responded remarkably to local roentgenotherapy. The effect of the drug on the hematopoietic system is difficult to evaluate because of the almost constant use of transfusions. Nevertheless, definite improvement was obtained in the peripheral blood by prednisone alone, as shown by the values of both the red blood and the white blood cells. Complete normalization of the blood picture was even obtained in 2 patients. Stress must be laid on the excellent quality of the remissions from the functional point of view, which gave the patients a feeling of complete recovery.

A Toxic Agent in the Etiology of Leukemia. R. Scheuer-Karpin. Ztschr. ges. inn. Med. 12:416-423 (June 15) 1958 (In German) [Leipzig, Germany].

The author reports on clinical observations made on 40 patients with granulocytopenia or acute myelosis at the first clinic for internal medicine of the Hufeland Hospital in Berlin-Buch. Of these 40 patients, 14 had taken dimethylaminophenyldimethyl-pyrazolon (Pyramidon), 6 acetophenetidin (Phenacetin), and 8 various other medications, such as methylthiouracil, phenolphthalein, quinacrine hydrochloride (Atabrine), and analgesics. Twelve had taken no medication as far as could be determined. Examination revealed that toxic granulocytopenia and acute myelosis are always associated, since they have a common etiology. Granulocytopenia may develop into acute leukosis if the patient lives long enough. Hypercellular bone marrow with numerous immature forms in a patient with granulocytopenia is not a sign of regeneration, and the prognosis in such a patient is not favorable, for in most cases acute myelosis has been found later. The administration of Pyramidon in combination with other etiological agents can produce granulocytopenia and then myeloblastic leukemia. Phenacetin and its derivatives are suspected of causing similar blood dyscrasia.

Severe Effects of Influenza Virus Infection. J. A. Forbes, M. J. Australia 2:75-79 (July 19) 1958 [Sydney].

The Asian, type A, influenza epidemic in Melbourne, Australia, prompted the author to make a study of 672 patients admitted to Fairfield Hospital in that city during July and August, 1957. These patients showed clearly some of the relatively infrequent, more severe effects of influenza virus infection. Of the 672 patients, 169 had uncomplicated influenza, with a great variety of symptoms. About 120 of these complained of severe headache, often associated with generalized aches and pains, and in 31 patients the combination of headache and meningism was such that lumbar punctures were performed revealing normal cerebrospinal fluid. No evidence was thus found of direct cerebral or meningeal involvement by the influenza virus. One hundred twenty-seven patients were admitted to hospital with severe laryngeal obstruction, 93 of them being children, aged 9 years or less. Influenza in young children may well predispose to secondary bacterial laryngotracheobronchitis; it can accelerate the obstruction of the airways, for they are small and likely to be impaired by the inflammation and edema which are produced by a pathogen with a predilection for respiratory epithelium and lymphoid tissue. The remaining 376 patients were admitted with pneumonia. Although younger patients predominated in this group, bacterial complications were proportionately more frequent among those over 40 years of age.

It was considered that the over-all isolation rate of pathogens from all the patients of this study provided a useful practical index of the causative agents as a basis for the initial treatment of these patients. It was apparent that the commonest pathogenic agent was Diplococcus pneumoniae, and this was confirmed by the clinical details, by x-ray appearances, and even by postmortem findings which showed it to be most commonly involved in death. Streptococcus, group A, appeared to be the next important causative agent, and Staphylococcus organisms were involved to a minor extent. Penicillin was used alone in the treatment of 82 patients who were admitted at an early stage of the disease. Tetracycline was combined with penicillin in the treatment of 201 patients in whom a broader antibiotic spectrum seemed desirable. According to subsequent bacteriological findings, combinations of penicillin, streptomycin, erythromycin, and Chloromycetin were used in those patients in whom

it was considered that delay in the selection of the appropriate antibiotic would result in death. Adult patients with severe pneumonia were given 2 million units of penicillin every 2 hours; it was apparent that these large doses caused more rapid subsidence of fever and toxemia than did the administration of 1 million units every 6 hours.

Thirty-eight deaths occurred among the 672 patients. Most patients died as a result of associated diseases, such as congestive cardiac failure, cerebrovascular accidents, nephrosclerosis, emphysema, and myocarditis. Twelve of the 38 patients died of severe pneumonia. These data suggest that the influenza virus (Asian, type A) infection caused death occasionally in the absence of associated bacterial infection, while the severity of the secondary pneumonia suggested that without antibiotics, and particularly without penicillin, the mortality rate would have been even higher.

Hyperventilation Syndrome. J. Calvo Melendro and P. Sánchez-Malo Calvo. Rev. clín. españ. **69**:205-210 (May 31) 1958 (In Spanish) [Madrid].

The syndrome of spontaneous (or idiopathic) pulmonary hyperventilation is of psychic origin. It is mainly due to emotions and linked to anxiety. It can be either acute or chronic. The predominant symptom is hyperpnea, which appears in association with dizziness, a feeling of emptiness of the head, cloudy state of the mind or complete loss of consciousness, certain sensorial and digestive signs, tachycardia, and precordial pain. In the course of the attack the arterial blood pressure falls; the electrocardiogram shows extrasystoles and abnormalities of the S-T segment and of the T wave, signifying a diminished output of the left ventricle. The electroencephalographic tracings are also changed. A diagnosis is made by the results of the pathognomonic test, which consists of the induction of provoked hyperpnea. The test is made by having the patient breathe deeply at a rate of 40 respirations a minute. In the presence of the syndrome a typical attack occurs within 15 or 30 seconds. In normal persons the test gives negative results even after 3 minutes. The contratest consists in making the patient breathe into a paper bag during an attack, thus compelling him to rebreathe his own expelled air. By these means the attack is aborted, and the act of breathing becomes normal within 15 or 20 respirations. The syndrome is frequent in women and rare in men.

The authors report 6 cases of hyperventilation syndrome in women, between the ages of 27 and 37 years. In all the patients the test of provoked hyperpnea and the contratest gave positive results. Emotions, excessive physical work, or mental anxiety were the eliciting factors of the attacks, which were repeated at very long and irregular intervals of time. In all the patients, also, the attacks lasted for a period that varied between 1 hour and 24 hours, during which more or less subdued hyperpnea continued. The hyperpnea stopped only if the attack ended, if the patient became unconscious, or if the contratest was carried out. The authors believe that the syndrome is caused by associated circulatory disturbances and disturbances of the centers of respiration. The main circulatory disorders involved in the development of the syndrome are an increased reflux of venous blood to the heart and a diminished arterial blood pressure.

Five-Year Follow-Up Study of Patients with Bleeding Duodenal Ulcer with and without Surgery. R. M. Donaldson, J. Handy and S. Papper. New England J. Med. **259**:201-207 (July 31) 1958 [Boston].

Of the 1,149 clinical records of patients admitted to the Cushing and Boston Veterans Administration hospitals with conditions classified as "duodenal ulcer with hemorrhage," "gastrointestinal hemorrhage" without other symptoms, and "duodenal ulcer," 142 were selected for study, as they presented indubitable evidence of gastrointestinal bleeding and duodenal ulceration. Each of the patients had had one or more of the following: black stools (positive guaiac test), hematemesis, bloody gastric aspirate (positive guaiac test), and roentgenographic demonstration of a deformed duodenum or a definite ulcer. For purposes of study the patients were divided into 2 groups. The first group consisted of 100 patients who were first seen during their initial episode of gastrointestinal bleeding; the second group consisted of 36 patients who gave a history of one or more previous gastrointestinal hemorrhages. Before their present admissions, 71 patients had received transfusions of whole blood, and in 61 cases a diagnosis of duodenal ulcer had been made by x-ray examination; 22 patients, however, had not experienced abdominal pain or any other symptoms referable to the gastrointestinal tract. Roentgenographic confirmation of duodenal ulcer was accomplished in 127 patients, duodenal-bulb crater in 73, deformed duodenal bulb in 46, and postbulbar ulcer in 8.

Of the 100 patients in the first group, 38 suffered hemorrhage within 5 years of the initial episode, 10 of the patients bleeding on more than one occasion. Of the 13 patients operated on during the initial episode, bleeding was the major indication for surgery in 11, and associated pyloric obstruction in 2. An additional 25 patients were subjected to subtotal gastrectomy sometime during the 5-year period. Eleven of the 100 patients died within 5 years of the initial bleeding episode, 8 deaths being directly attributable to uncontrolled hemorrhage. Six of the deaths occurred during the initial hemorrhage, and 2 were due to proved gastrojejunal marginal ulcers developing 5 days and 2 months,

respectively, after gastrectomy. In the first group there were 37 survivors at the end of 5 years who had had neither gastrectomy nor recurrent hemorrhage, a number which was reduced to 32 almost 2 years later. Of the 36 patients in the second group, 15 had further bleeding episodes within 5 years of the initial episode. There were no deaths in this group in the follow-up period, and at the end of this period 10 patients still had had neither gastrectomy nor recurrent hemorrhage. Recurrent bleeding within a 5-year period occurred in approximately 40% of the patients not operated on. There was a significant recurrence of bleeding after subtotal gastrectomy, 10 of 48 patients operated on experiencing hemorrhage within 5 years of operation.

SURGERY

Mitral Commissurotomy: Fifty Consecutive Cases with No Operative Mortality. A. M. Sabety and H. M. Ewing. J. M. Soc. New Jersey **55**:418-421 (Aug.) 1958 [Trenton].

The authors report on their experience in the performance of 50 consecutive mitral commissurotomies without a single operative death. The present-day success of the surgical procedure is attributed to a better understanding of the abnormal physiology of mitral valvular stenosis and its alteration toward normal by surgery and to the tremendous strides that have been made in the selection of patients, operative technique, preoperative and postoperative care, and anesthetization. For purposes of classifying patients as to need for commissurotomy, those in this series have been divided into 4 groups: (1) patients who were asymptomatic, 0; (2) patients whose main symptom was dyspnea, 20; (3) patients with pulmonary hypertension, 26; and (4) patients with chronic right-heart failure, 4. An appreciable amount of calcification was found in 9 patients; no calcification was found in 19 patients; a regurgitant jet was noted in 13 patients; and 36 patients were operated on during chronic atrial fibrillation. The operative technique was essentially that which has become routine procedure in mitral commissurotomy; it emphasizes meticulous attention to every detail in opening the stenosed valve to its fullest extent and separating the chordae tendineae if they are found to be fused.

Failure and Replacement of Abdominal Aortic Grafts. M. R. Gaspar. Am. J. Surg. **96**:202-212 (Aug.) 1958 [New York].

The author reports on 5 men, between the ages of 55 and 75 years, 4 of them with aneurysm of the abdominal aorta and 1 with thrombotic occlusion of the abdominal aorta, in whom grafts were used to bridge the defects resulting from the surgical removal of portions of the aorta. Nylon grafts were used originally in 2 patients and freeze-dried homografts in 3. Failure of the original aortic grafts occurred in all 5 patients. Thrombosis was the pathological process in the 2 patients with nylon grafts and in 1 patient with homograft. Failure occurred over a wide span of time, varying from the time of operation to 14 months after operation. Residual arteriosclerosis was the cause of failure of the 2 nylon grafts and 1 homograft. Obviously all of an aneurysm should be resected. Residual arteriosclerosis is more easily overlooked but must be removed or bypassed because it fosters occlusion of the graft. A poorly fashioned cloth synthetic graft was instrumental in the failure of the graft in 1 patient, thus showing that imperfect fashioning of grafts may be another cause of failure. Imperfect anastomoses also contributed to thrombosis within grafts. Defective freeze-dried homografts were the cause of failure in 2 of the 5 patients; in one patient the homograft ruptured at operation and in the other on the 4th postoperative day. Freeze-dried homografts appear to be unreliable unless some more satisfactory method of preparation is found. Four other ruptures of grafts were observed by the author, 2 in patients in whom freeze-dried human aortic grafts were used and 2 in cases of freeze-dried dog homografts. Synthetic grafts have not shown a tendency to rupture.

When abdominal aortic grafts fail, the entire grafts should be replaced. Bifurcation homografts were used for replacement in 2 of the 5 patients in whom the original grafts had failed, and thoracic aortic homografts were used for replacement in 3. Thoracic aortic homografts provide a larger diameter than bifurcation grafts and can be fitted more easily at the proximal end of the anastomosis. The replacement was successful in 4 of the 5 patients. Although this series is small, these results suggest that an attempt should be made to replace abdominal aortic grafts which fail. Additional years of observation will show which material is to be considered the best graft material for arterial substitutes.

The Outlook of Vascular Surgery Upon the Aged. C. R. Hitchcock and T. O. Murphy. Journal-Lancet **78**:329-335 (Aug.) 1958 [Minneapolis].

Of 260 patients with vascular disease operated on at the University of Minnesota Hospitals and the Minneapolis General Hospital up to Sept. 1, 1957, 250 (96%) were 55 years of age or older. There were 150 patients with occlusive arterial disease; of these, 107 (71%) were between the ages of 60 and 75 years, and 29 (18%) were between the ages of 75 and 90 years. One hundred ten patients were operated on for arterial aneurysm; 74 (67%) of these were between the ages of 60 and 75 years,

and 25 (22.7%) were over 75 years of age. In 83 (76%) of the 110 patients operated on for correction of a major arterial aneurysm, the procedure was successful. In the 18 patients operated on for ruptured aneurysm, 14 deaths occurred, and successful repair was done in only 4 (29%). Of the 92 patients operated on electively for aneurysms, only 10 died and the operation was successful in 80 (87%). These data emphasize the significant difference in the success rate of resection of aortic aneurysms in the elective stage as compared with the ruptured stage. Of the 150 patients who were operated on for segmental occlusive arterial disease and in whom bypass shunt grafts were used, the operation was successful in 16 (82%) of 21 patients with aorta-femoral bypass shunts, in 58 (79%) of 74 patients with femoral-popliteal bypass shunts, and in 2 patients with popliteal bypass shunts. The bypass type of arterial reconstitution is easier to accomplish technically than an in-line graft establishing direct continuity of the blood flow, since the arteries involved in the extremities are usually relatively normal, and end-to-side anastomoses are done with ease. The important small collateral arteries are not damaged by the bypass shunt technique; in the event of a subsequent thrombosis of the bypass shunt graft, the original vascular supply to the extremity is not significantly damaged, and the extremity, therefore, is not jeopardized.

These findings emphasize the tolerance of the elderly patient toward extensive vascular surgery. With advanced methods of anesthesia and prevention of hypotension during and after the surgical intervention, the results appear to be excellent. Arterial wounds and skin incisions in such patients have healed rapidly, and usually hospitalization has not been required longer than 14 to 18 days. The current surgical approach to serious vascular disease, a palliative one in the over-all problem of the treatment of arteriosclerosis, has a significant part to play in the attempt to prolong the life of patients in a manner permitting maximum usefulness of all their faculties.

Repair of Injury to the Common Bile Duct: Results in 69 Cases. G. L. Hoffman and G. Crile Jr. Cleveland Clin. Quart. **25**:126-132 (July) 1958 [Cleveland].

Between 1950 and 1955, 89 operations for injured bile duct were performed at the Cleveland Clinic Hospital, of which 69 (performed on 58 patients) were classed as reparative. Of the 69 reconstructive procedures, 21 were hepaticoduodenostomies; 19 were simple dilatations with insertion of a T-tube; 12 were end-to-end anastomoses; 7 were hepaticojejunostomies; 5 were Roux-Y procedures; and 5 employed either a Vitallium-tube prosthesis, a skin grafting, or the Grindlay procedure. The best results were obtained in the first group (hepaticoduodenostomy), in which 18 patients were classified as having obtained good results—feeling well with no chills, fever, or jaundice. Two of the 3 patients in the first group, in whom operative results were not good and who had intermittent symptoms of cholangitis without jaundice, subsequently underwent gastric resection (Billroth 2) to exclude the biliary tract from the direct alimentary flow. The remaining procedures produced satisfactory results in less than 60% of the cases. The simplest approach to the damaged bile duct is through a subcostal incision, dissecting the undersurface of the liver from right to left. Fine chromic catgut is the suture material of choice. The most acceptable type of internal splint is the standard T-tube which, whenever possible, should be brought out through a separate opening and not through the anastomotic line, as is done when the stump of the proximal part of the duct is short.

Clinical Experiences with the Surgical Treatment of Acquired Aortic Vascular Disease. O. Gwathmey, H. C. Pierpont and B. Blades. Surg. Gynec. & Obst. **107**:205-213 (Aug.) 1958 [Chicago].

A series of 53 patients with a variety of aortic vascular lesions treated during the past 4 years is reviewed in an attempt to correlate the authors' earlier impressions concerning the restoration of the aorta with more recent concepts. A total of 14 aneurysms involved all or part of the aortic arch. Syphilis was the etiological agent in 6, atherosclerosis in 3, and trauma in 3, the agent being undetermined in 1. The following adjunct techniques were used: hypothermia, staged segmental occlusion, and extracorporeal circulation. Three of the 14 were classified as emergency cases. Homologous freeze-dried grafts were used in 8 cases, while 2 cases required only aneurysmorrhaphy; 3 patients died prior to the grafting stage, and 1 patient was considered inoperable. There were no late complications in this group. Four patients were discharged as improved and are at present alive and well at 45, 44, and 30 months and 2 weeks after the operation. There were 3 delayed complications, and 7 cases were classified as immediate complications. There were 3 cases of aneurysm of the descending thoracic aorta—2 fusiform and 1 saccular lesions. A homologous and Vinyon "N" graft was used in 1 case, and Vinyon "N" and Orlon grafts were implanted in the other 2 cases. Hypothermia was used as an adjunct technique in 2 cases, and the aorta was cross-clamped under normothermic conditions in the other case. There were 2 late complications in this group and 1 immediate complication.

Thirty-seven patients with acquired lesions of the abdominal aorta were operated on. Thirty-two of these lesions were true aneurysms, all of them be-

ing basically fusiform in type but having saccular components superimposed. The etiological factor prevailing throughout the entire group was atherosclerosis. Thirty-five patients had resection of the diseased aortic segment with grafting. The only adjunct technique was hypothermia, which was used in 1 case only. Five types of grafts were used —homologous, Dacron, nylon, Orlon, and nylon crimp. Approximately 86% of the 35 abdominal lesions were aneurysms, the remaining 14% being due to thrombo-occlusive disease. In the elective group of 16 aneurysms there were only 3 complications (1 immediate, 1 delayed, and 1 late), in contradistinction to the 14 complications (4 immediate, 9 delayed, and 1 late) in the emergency group of 16 cases. In the 5 cases of thrombo-occlusive disease there were 3 immediate complications and 1 delayed complication. Thrombosis occurred in all 3 patients of the immediate group who underwent reexploration with reestablishment of circulation and required still a third procedure. Thrombosis as a complication in abdominal grafts occurred more frequently in thrombo-occlusive disease than in aneurysmal lesions.

Multiple Epiphysial Dysplasia. H. Barrie, C. Carter and J. Sutcliffe. Brit. M. J. 2:133-137 (July 19) 1958 [London].

Fairbank defined multiple epiphysial dysplasia as "a rare developmental error characterized by mottling or irregularity in density and outline of several of the developing epiphyses, dwarfism, and stubby digits." Symptoms invariably begin in childhood, the youngest recorded case being that of a 19-month-old infant. In the present series the ages ranged from 2 to 71 years. The most prominent symptoms are joint pain and stiffness with a variable degree of disability. Since the lesions are multiple rather than generalized, symptoms predominate in specific joints, the hip and knee joints being the most commonly affected as they are the most liable to weight-bearing strain. The distribution of symptomatically involved joints does not necessarily parallel the roentgenographic distribution, which is more often than not severest in the epiphyses of the wrist, hands, and ankles. The degree of disability varies from slight discomfort to marked impairment of function, and although the changes in the epiphyses are permanent, the symptoms are characteristically transient and fluctuating. Osteoarthritis is an inevitable complication, and severe hip trouble may cause difficulty in natural childbirth. Similar symptoms and signs as well as roentgenographic features prevail in affected members of the same family. The familial pattern suggests that dominant genes are responsible for all examples of the disorder, although more than one mutation would seem to be necessary to explain the differing degrees of severity in different families. Patients who receive physical therapy early in life are afforded considerable relief at the time and subsequently develop less disability.

A New Therapeutic Concept of the Exstrophied Bladder. C. S. Snyder. Plast. & Reconstruct. Surg. 22:1-10 (July) 1958 [Baltimore].

The author reports on 2 boys, aged 1 year and 6 months, respectively, who were operated on for exstrophy of the urinary bladder. The intestinal tract was prepared with a combined sulfo-neomycin medication 3 days before the surgical intervention, and enemas were given 2 days before the operation. With the aid of general endotracheal anesthesia, the abdomen, perineum, buttocks, and thighs were surgically cleansed and aseptically draped. A catheter was placed in each ureter. The bladder was dissected from the abdominal wall, isolating the ureters and preserving the vesical blood vessels. The rectum was elevated from the posterior part of the pelvic wall, and a site of transection was selected 2 in. above the anal outlet. A fenestration was made in the posterior part of the bladder wall between the ureters, and the distal end of the rectal segment was coapted to it with 2 layers of sutures. The ureteral catheters were brought through the anal orifice by way of the new urinary rectal receptacle. An incision was made posterior to the anal outlet but within the external and internal anal sphincters. The proximal end of the rectal segment was pulled through the levator ani sling and within both anal sphincters. It was sutured to its recipient site, leaving a redundancy of intestine present externally. The bladder was closed over an indwelling catheter which was brought through the abdominal wall. The abdomen was closed in layers without tension. Each patient lost approximately 150 cc. of blood, which was replaced during the operative procedure. On the second postoperative day the ureteral catheters were removed, and the next day the remaining indwelling catheter was extracted. Both patients had uneventful recoveries.

The fact that due to this operation the urinary stream is completely separate from the fecal discharge is of definite advantage, as it eliminates ascending renal infection which has been the most common complication of operative procedures previously in use. There is no problem of ureteral obstruction at a site of anastomosis, because the ureters are left intact to empty their contents as they should into the bladder. The patients of this report have been followed for 1 year postoperatively, and no complications have occurred to give reason that these 2 boys operated on for bladder exstrophies should not enjoy a normal life expectancy. Two other patients have been operated on since the author's paper was submitted for

publication, and both are doing well. Follow-up intravenous pyelograms have illustrated normal functioning genitourinary tracts.

Operations for Extreme Mitral Stenosis in Patients over 45 Years of Age: Preoperative and Postoperative Study of 35 Cases. P. Soulié, F. Joly, P.-E. Gareau and P. Corone. Arch. mal. cœur **31**:616-625 (July) 1958 (In French) [Paris].

The authors report on 26 women and 9 men, between the ages of 45 and 54 years, with extreme mitral stenosis in that the mitral orifice was reduced to a cross sectional area 1 sq. cm. or less. Although all the patients had had moderate dyspnea on effort for a prolonged period varying from 2 to 20 years, their activity was hardly impaired until the clinical and hemodynamic symptoms of mitral narrowing became much more severe after the age of 40. Pulmonary edema on effort or subacute edematous attacks were observed in 31 patients. Hemoptysis occurred in 11 patients, and bloody sputum was observed in 6. Pulmonary embolism occurred in 7 patients and other systemic embolic attacks in 5. Complete arrythmia was noted in 20 patients. Signs of overload on the right ventricle were revealed by the electrocardiograms obtained from 31 patients. The volume of the heart was increased in 23 patients, and the pulmonary arteries were dilated in all the patients. The pressure in the pulmonary capillaries varied between 20 and 30 mm. Hg. The pressure in the pulmonary arteries also was increased; the systolic pressure varied between 80 and 140 mm. Hg in 12 patients, and the average pressure was above 50 mm. Hg. Commissurotomy was performed with the knife on 24 patients and by digital fracture on 11. Three patients died, 2 of ventricular fibrillation in the course of surgical intervention and 1 of cardiac decompensation 3 months after the operation.

The 32 patients who survived the operation were followed for 9 to 24 months. Functional disturbances subsided in varying degree in almost all of them. Pulmonary edema disappeared and hemoptysis did not occur. Dyspnea on effort was completely absent in 13 patients, nearly completely in 10, and partly in 9. Postoperative electrocardiographic changes were studied in 27 patients. Four of these had not shown preoperatively signs of overload on the right ventricle, and their postoperative electrocardiograms were not changed. Of the remaining 23 patients, the condition of 19 was improved in that there were less signs of overload on the right ventricle, and only 4 were not improved. Most improved were those in whom the preoperative overload on the right ventricle had been most pronounced. Of 15 patients who underwent catheterization postoperatively, the pressure in the pulmonary capillaries was reduced by 12 to 20 mm. Hg in 10 and by 7 to 10 mm. Hg in 3; the pressure in the pulmonary arteries also was reduced in all these patients, and it was restored to normal in 3. Two patients did not show hemodynamic improvement because of a systolic reflux which had become more pronounced.

These observations show that the results of commissurotomy, performed on patients in the 5th and 6th decades of life when moderate mitral narrowing has become more severe, remain satisfactory. It might be that the operative risk is somewhat greater and that complete regression of the hemodynamic and electrocardiographic symptoms may occur less frequently than in younger patients, but the differences are not significant. Such patients should, therefore, not be denied surgical intervention because of their advanced age alone.

NEUROLOGY & PSYCHIATRY

Pelizaeus-Merzbacher Disease: A Clinical Study. H. R. Tyler. A. M. A. Arch. Neurol. & Psychiat. **80**:162-169 (Aug.) 1958 [Chicago].

The author reports the cases of 3 Negro boys, between the ages of 9 and 16 years, with a slowly progressive hereditary form of cerebral diplegia characterized by early development of nystagmus, ataxia, and spasticity. The 3 patients were brothers and belonged to a large family in which 27 members in 7 generations were affected with this disease in a fairly stereotyped and predictable manner. The disease was always transmitted through an unaffected female, and the affected male never reproduced. No female member with the disease was known. If the male was not affected, then his children, including the daughters, did not reproduce the disease. About 50% of the females had affected children, but the cases of the 3 boys were the only definitely known ones. Other members of the family called these affected persons "head nodders" and "eye waggers." The condition was usually observed about 8 to 10 days after birth, and sometimes as late as 3 months. The parents noted that the eyes were constantly moving and that the head was moving in a repetitive side-to-side tremor. The children were hypotonic and rarely learned to sit or stand. Placing reactions were usually lost by 18 months of age. Some of the patients could propel themselves by a peculiar writhing, snake-like motion of the body, with head held extended. This was the only demonstration of a righting reflex noted. By the age of 3 to 6 years, kyphoscoliosis, spasticity in the lower extremities, athetosis, intention tremor, and slight regression in the mental state were noted. The upper extremities became slightly spastic by the age of 10 to 12 years. Thin arms and legs were noted in some members of the family. The rate of progression of the disease seemed to become slower and slower with each year until it appeared almost as though, in some

of the older affected persons, it occasionally became stationary. Most of the patients died of intercurrent infections in early years. One lived to 51 years of age.

The symptoms of the patients in this study were those of diffuse sclerosis of the subcortical white matter, which were first described in 14 members of a family by Pelizaeus and Merzbacher, after whom the disease has been named. The only points of difference between the 2 families with this rare hereditary disease were that the pattern of onset of symptoms appeared more rigid in Tyler's patients, that none of the female members were affected in contrast to 2 females in the original family, and that remissions were less obvious in the original family. The early development of nystagmus and other brain-stem signs distinguishes the illness from the familial forms of Schilder's disease (progressive subcortical encephalopathy) and metachromatic leukoencephalopathy.

Lobotomy: A Fifteen-Year Study. A. McCausland and D. M. Wickware. Canad. M. A. J. **79**:168-170 (Aug. 1) 1958 [Toronto].

Two hundred patients who had been subjected to a standard bilateral lobotomy have been followed for 3 to 15 years. The age range of the patients, 146 females and 54 males, was from 18 to 77 years, the greater number of patients falling in the 30-to-59-year age group. The average length of time from onset of illness to operation was 143.6 months, while the total hospital stay prior to operation averaged 47 months. The mortality rate to date for the entire series of 300 cases has been 0.3%. Schizophrenia accounted for a greater proportion of failure and a correspondingly lesser degree of improvement than did manic-depressive psychosis. The results for involutional melancholia and schizoaffective psychosis cannot be accurately assessed because of the small number of patients in these groups. Classification by age group indicates that results were better for patients in the 40-to-59-year age group and less favorable for the 20-to-39 and 60-to-70-and-over age groups. The latter results would seem to reflect the preponderance of schizophrenic disorders in the 20-to-39-year age group.

Anorexia Nervosa: A Somatic Disorder. E. Williams. Brit. M. J. **2**:190-195 (July 26) 1958 [London].

The author reports on 53 female patients, between the ages of 12 and 40 years, with anorexia nervosa who were admitted to the London Hospital; 49 were admitted between 1897 and 1953, and 4 between 1953 and 1957. Marked weight loss and amenorrhea were present in all. Despite extensive investigation, none showed evidence of primary organic disease. The patients were hospitalized for periods ranging from 7 to 130 days, except one patient who was comatose on admission and who died the next day. Few patients were confined to bed, and for most of them no special diets were prescribed. Renourishment of 7 patients was accomplished by feeding with the stomach tube, and in these patients the immediate results were so good that on discharge each had gained, on the average, 22 lb. (10 kg.). Of the 46 patients who were not treated with intubation, 7 gained more than 14 lb. (6.4 kg.) in weight while in the hospital, but the weight was restored to normal in only 5 of these. The other 39 patients in this group gained, on the average, only 9 lb. (4.1 kg.) per patient.

Seven of the 53 patients who were treated for anorexia nervosa were lost to follow-up. Of the 46 patients who were followed, 10 have died, 3 have not improved, 6 have improved, and 23 have completely recovered. It is still too early for an evaluation of the 4 patients who were admitted after 1953, but they have all been treated with intubation which is the most effective in-patient treatment. The deaths of 8 of the 10 patients who died resulted solely from malnutrition. Other patients who were just as severely undernourished recovered spontaneously after having been refractory for a varying number of years. They resumed eating of their own volition, mostly after their environment had deliberately or accidentally been changed.

Promising Results in Cryptococcal Meningitis. H. Rubin and M. L. Furcolow. Neurology **8**:590-595 (Aug.) 1958 [Minneapolis].

The authors report on their experience in the treatment of 10 cases of cryptococcic meningitis with Amphotericin B. Cryptococcus neoformans was isolated from the spinal fluid of all the patients and from the skin lesions of 2 patients. The pathogenicity of all isolated strains was confirmed by the demonstration of capsule formation and growth of budding yeast forms at 37 C; 9 of the 10 isolated strains were also shown to be pathogenic for mice, with the development of hydrocephalus after cerebral inoculation. Amphotericin B was administered intravenously to all the patients in doses ranging from 50 to 100 mg. for a total dose of 1.4 to 3.7 Gm. Eight of the 10 patients are alive at follow-ups ranging from 2 to 14 months. In the 2 fatal cases both patients were comatose and moribund before treatment and never regained consciousness. Two of the surviving patients are pursuing normal activities and have normal spinal fluids which have remained sterile upon repeated culture; 3 patients have shown clinical improvement with either normal or improved spinal fluid indexes; 1 patient has remained stable in spite of previous long-standing central nervous system disease; and 2 patients have suffered relapses. Toxic side-reactions to Amphotericin B have been minimal, although therapy was suspended in one patient because of symptoms ascribed to liver toxicity. Chemical

phlebitis occurred. Fever, chills, and nausea sometimes accompanied the initial intravenous infusion but were diminished or avoided by premedication. The most promising finding, upon evaluation of therapy, is the consistent sterility of the spinal fluids in 7 of the 8 surviving patients.

Intracranial Hemorrhage in Cerebral Arteriovenous Anomalies. M. W. Wood and H. J. Svien. A. M. A. Arch. Neurol. & Psychiat. 80:170-172 (Aug.) 1958 [Chicago].

Of 51 patients with cerebral arteriovenous anomalies which were revealed either at surgical intervention or by angiography at the Mayo Clinic, 16 patients, 8 male and 8 female, between the ages of 6 and 60 years, had 20 attacks of subarachnoid hemorrhage. The average age at the time of hemorrhage was 31 years. Three of the 16 patients had more than 1 attack of bleeding, 1 having 3 attacks and 2 having 2 attacks each. In all 20 episodes the patients had severe headache at the onset, and nausea and vomiting appeared early in about two-thirds. The patients were unconscious in 8 of the 20 attacks of hemorrhages, and in 2 of the 8 for less than 1 day. Recovery occurred in 6 of the 8 instances, but 2 patients died during the hemorrhage. Seven patients had no definitive surgical treatment for their lesions. The 2 deaths from subarachnoid bleeding which occurred in this group gave a mortality rate of 12.5% for the entire series, which was about the same as that reported by other workers. No bleeding recurred for 7 to 16 years in the other 5 patients who were not surgically treated for their lesions. Of these 5 patients, 3 have no residual paralytic or speech defects, but 2 have some degree of residual hemiparesis. Nine of the 16 patients were treated surgically. No deaths from bleeding occurred in this group, but 4 of these patients have had attacks of subarachnoid bleeding since operation.

Although this group of 16 patients with intracranial hemorrhage is small, certain characteristics of bleeding from arteriovenous anomalies can be deduced as follows. The bleeding from a cerebral arteriovenous anomaly is not nearly as fulminating as that from a cerebral aneurysm; bleeding from an arteriovenous anomaly is not nearly as likely to be fatal as that resulting from a ruptured cerebral aneurysm. Residual neurological deficit is neither frequent nor often profound.

It is generally conceded that subarachnoid bleeding from a cerebral aneurysm is an indication for surgical treatment in patients who survive the initial attack and in whom such factors as age are not contraindications. Subarachnoid bleeding from an arteriovenous anomaly does not have the same ominous connotation as that resulting from a cerebral aneurysm. Hence, one must be cautious in considering subarachnoid bleeding from an arteriovenous anomaly as an indication for surgical removal of the lesion. Another reason for caution is the appreciable operative mortality rate. Furthermore, even though total excision is thought to have been accomplished at operation, long-term follow-up observations may prove this to be untrue, leaving the same set-up for bleeding as before. It should be kept in mind that the residual neurological deficit in most of the surgically treated patients is bound to be appreciable because of the frequent location of the anomaly in the vicinity of the Sylvian and Rolandic fissures.

GYNECOLOGY & OBSTETRICS

Progesterone-Induced Withdrawal Bleeding as a Simple Physiologic Test for Pregnancy. G. E. Hayden. Am. J. Obst. & Gynec. 76:271-278 (Aug.) 1958 [St. Louis].

The author presents a study on the differentiation of early pregnancy from secondary amenorrhea of short duration. The use of progesterone as a diagnostic and a therapeutic agent in the management of amenorrhea has been evaluated, and the application of progesterone-induced withdrawal bleeding as a diagnostic test for pregnancy has been employed in 102 women whose ages ranged from 18 to 35 years. The patients were selected only on the basis of previously regular menstrual periods and the distinct possibility that a conception had occurred. They were amenorrheic for 35 to 70 days. Forty-four patients were given anhydrohydroxyprogesterone orally in a dose ranging from 200 to 400 mg. per day for 4 or 5 days. In 43 patients progesterone, U.S.P., was administered vaginally in a dose ranging from 75 to 250 mg. per day for 4 or 5 days, and in 15 patients 17-alpha-hydroxyprogesterone caproate was injected intramuscularly in a dose ranging from 125 to 500 mg. per day for 2 to 5 days. Sixty-four patients failed to respond, and pregnancy was confirmed in each instance. All the pregnancies continued uneventfully, and normal-term infants resulted. In 38 patients withdrawal bleeding occurred. In 23 (85%) of 27 patients who had received progesterone preparations either by mouth or vaginally, the onset of withdrawal bleeding occurred between the 3rd and the 7th day from the day of cessation of medication. In 8 (72%) of 11 patients to whom the progesterone preparation had been administered intramuscularly, the onset of withdrawal bleeding occurred between the 8th and the 14th day; in 1 patient the onset occurred even on the 16th day. Thus, the oral or vaginal mode of administration may be preferred to the intramuscular route. The amount and duration of bleeding could not be correlated with the mode of administration or amount. No alteration in the course of pregnancy was noted with either standard or ex-

cessively large dosage. Of 36 patients on whom follow-up examinations were carried out, 26 (72%) returned to normal menstrual cycles, and no further evaluation or therapy was indicated or needed. Two patients were lost to follow-up. Thus, because of its diagnostic as well as its therapeutic value, progesterone may be used even more extensively in patients with the brief or functional type of amenorrhea.

Current Treatment of Carcinoma of the Cervix. H. L. Kottmeier. Am. J. Obst. & Gynec. 76:243-251 (August) 1958 [St. Louis].

According to Kottmeier, the intracavitary radium treatment for carcinoma of the cervix must be individualized. Thus, the radium application in a patient with a narrow vagina should be quite different from the application in a patient with a large vagina; the intrauterine application of radium is to a much greater extent responsible for the dosage in the paracervical tissue and in the pelvic nodes than is the vaginal application of radium, and the contrary is true as far as the paravaginal spread of the cancer is concerned. This applies to cases of endocervical carcinoma or to those with a paracervical spread of the neoplasm. The intrauterine dose of radium should be considerably increased in such cases and the vaginal dose decreased. Thus, in a case of endocervical carcinoma, stage 1, the application of radium should be quite different from that in a case of disk-shaped carcinoma in the part of the uterine cervix which protrudes into the vagina.

The current individualized technique was started in 1949 at the Radiumhemmet in Stockholm. The treatment time was determined in the individual case by a direct reading of the dosage in the posterior wall of the bladder and the anterior wall of the rectum. A small ionization chamber contained in a curved probe was inserted first in the bladder and then in the rectum to a depth of 14 cm. With the probe in the midline and with gentle pressure on the wall, it was slowly withdrawn, and the dosage rate at each centimeter of distance was recorded. With the high intensity used, the optimal dose in the bladder was about 5,500 gamma r and in the rectum 4,000 gamma r, provided that attention was given to the dosage in an area of 3 cm. or more. A higher dose would increase the risk of proctitis or bladder damage. Overradiation of normal tissue should be avoided. Fractionated irradiation was preferable.

In uncomplicated cases, the intracavitary application was divided into 2 treatments, with an interval of 3 weeks. In infected cases, it was expedient not to apply the intrauterine and vaginal doses of radium simultaneously. In cases of endocervical carcinoma, of spread of the cancer to the paracervical tissue, and of pelvic lymph node metastases, an increase in the intrauterine dose was desirable. This might be realized by an increase in the time the radium was left in place or by an increase in the amount of radioactive material applied. From 100 to 200 mg. of radium was inserted into the uterine cavity, depending on the length of the sound. The diameter of the applicator was increased in order to avoid necrosis in the uterine wall. The application was controlled by the probe inserted into the rectum. It was preferable not to exceed a dosage of 2,500 gamma r in 24 hours to the anterior wall of the rectum and, furthermore, not to give external radiotherapy immediately after such an application. Additional roentgentherapy was given to the pelvic wall of every patient from 2 anterior and 2 posterior portals. The dosage ranged from 2,000 to 2,400 r in 24 to 32 days, although sometimes it was desirable to increase the dose to the pelvic wall. Prior to this additional therapy, however, a urovenogram was required for the purpose of obtaining information on pelvic anatomy. The marked improvement in the results obtained with this type of therapy supports the importance of individualization.

One thousand eighty-one patients were treated in Stockholm during the 3 years from 1949 to 1951. The oldest patient was 96 years of age, with a stage 1 carcinoma. Fifty-three patients were 30 years of age or younger. Palliative radiotherapy, i. e., one radium treatment or a few x-ray treatments, was given in 7.4% of the cases. Radical hysterectomy was carried out later in 43 cases of persistent or recurrent carcinoma, and fulguration was performed in 83 cases. The 5-year apparent recovery rate was 89.0% in stage 1, 64.4% in stage 2a, 45.2% in stage 2b, 33.5% in stage 3, and 7.8% in stage 4. Since 1949 a case has been allotted to stage 4 only if invasion of the bladder or rectum was proved histologically or distant metastases were present. Thus, the average 5-year cure rate was 51.1%, as compared with an average 5-year cure rate of 42.3% among patients treated between 1936 and 1945 and of 42.5% among those treated between 1946 and 1948.

The Importance of Highly Purified Bacterial Lipopolysaccharides for the Therapy of Inflammatory Diseases of the Adnexa. H. Fricke, V. Probst and G. Schumacher. Schweiz. med. Wchnschr. 88:691-698 (July 12) 1958 (In German) [Basel, Switzerland].

Whereas in the past vaccine preparations were chiefly used in nonspecific fever therapy, the authors are concerned with the use of the highly purified lipopolysaccharide Pyrexal that is extracted from Salmonella abortus equi. The preparation is free from protein and nucleic acid and consists largely (60%) of sugars and (40%) of lipids (lipid A). An intravenous injection of 0.1 to 0.2 mcg. of

Pyrexal produces a temperature increase of from 1 to 2 degrees (C). The temperature elevation appears after a latent period of 1 or 2 hours and subsides again from 6 to 8 hours after the injection. The pyrogenic threshold dose is the intravenous injection of 0.002 to 0.003 mcg. per kilogram of body weight. The fever-inducing effect gradually decreases after repeated injections, and so it becomes necessary to increase the dose gradually to insure the same effect. Pyrexal induces leukocytosis, activates fibrinolysis, and increases the serum properdin twofold to threefold.

The authors demonstrate on the basis of clinical studies that the intravenous administration of bacterial lipopolysaccharides produces excellent therapeutic results in the treatment of adnexitis. A comparison of the results obtained in 50 patients who were treated with the lipopolysaccharide Pyrexal with those obtained in 385 patients who were treated with the customary conservative methods demonstrated not only that the over-all results in acute and chronic cases were better with the intravenous fever therapy but that, in contrast to experiences in earlier years, patients treated during the acute and the subacute stage have better chances of recovery. In view of the anatomic and topographic peculiarities of the involved adnexa (small organ—large peritoneal surface) with extensive fibrinous exudates, adequate treatment of the inflammatory masses seems to depend on increase in resistance, on stimulation of the properdin system, on activation of the reticuloendothelial, leukocytic, and anterior-pituitary/adrenocortical systems, and particularly on the stimulation of fibrinolytic processes. The uniform course of the reaction that can be expected regularly after the intravenous injection of highly purified bacterial lipopolysaccharides greatly facilitates their clinical use. Side-effects usually take the form of headaches that can be readily controlled by suitable drugs. The occurrence of painful reactions at the site of the inflammation may be employed for differentiating adnexitis from tumors of the adnexa.

Treatment of Functional Uterine Bleeding with 17-Alpha-Hydroxyprogesterone Caproate (Efficiency and Limitations of Therapy). H. Zorn. Geburtsh. u. Frauenh. 18:924-933 (July) 1958 (In German) [Stuttgart, Germany].

The author reports on 224 female patients with functional uterine bleeding who were treated with a mixture of estradiol benzoate, estradiol valerate, and 17-alpha-hydroxyprogesterone caproate given parenterally. One hundred thirteen patients were admitted to the gynecologic clinic of the City Hospital in Berlin-Friedrichshain, Germany, and the remaining 111 patients were treated ambulatorily. Thirty-five of the 224 patients were immature girls, 35 were mature women, and 154 were at the termination of their reproductive period. Sixty-two patients received 125 mg. of hydroxyprogesterone caproate and 10 mg. of estradiol benzoate, 60 patients received 250 mg. of hydroxyprogesterone caproate and 10 mg. of estradiol benzoate, 24 patients received 375 mg. of hydroxyprogesterone caproate and 10 mg. of estradiol benzoate, 58 patients received 250 mg. of hydroxyprogesterone caproate and 10 mg. of estradiol valerate, and 20 patients received 250 mg. of hydroxyprogesterone caproate, 10 mg. of estradiol benzoate, and 10 mg. of estradiol valerate. Independently of the duration of bleeding before treatment and independently of the dosage employed, primary hemostasis was obtained within 24 to 36 hours as a rule, and within 48 to 60 hours at the latest, in 209 women (93.3%). The treatment failed in 5 patients, and in 7 additional patients bleeding was arrested later with conservative measures. Three women were lost to follow-up and were also considered as failures. Definitive arrest of bleeding without withdrawal bleeding occurred in 4 women, between the ages of 41 and 51 years; it may be assumed that an exclusive estrogen effect was exerted on an almost exsanguinated mucosa in these 4 patients. Withdrawal bleeding occurred in 201 patients within 10 days, on the average, and its course was uneventful in 189 (84.3%). Further intervention was not required. The withdrawal hemorrhage lasted, on the average, for 8 days. Failure of the treatment nearly always indicated an organic endometrial disorder as the cause of the hemorrhage.

Thirty-five women with histologically proved organic disorders, such as polyps of the uterine cervix or the body of the uterus, endometritis, and inflammatory processes of the adnexa associated with bleeding, were given the same treatment as the patients with functional bleeding. Arrest of bleeding occurred for a short time in 18 patients and was followed by withdrawal bleeding in some of them; the latter often was severe and prolonged. Administration of large doses of 17-alpha-hydroxyprogesterone caproate not only delayed the onset of withdrawal bleeding by 4 to 6 days but also markedly reduced the blood loss. With combined administration of 17-alpha-hydroxyprogesterone caproate and long-acting estradiol valerate, there was a delay before the hemostatic effects became manifest, but withdrawal bleeding was shortened by 2 or 3 days. The delay in the hemostatic effect may be prevented by the combined administration of estradiol benzoate and estradiol valerate with 17-alpha-hydroxyprogesterone caproate. Although treatment with the estradiols and 17-alpha-hydroxyprogesterone caproate had beneficial effects in patients over 45 years of age, the author cautions against its routine use in these patients unless microscopic examination has excluded the possibility of carcinoma. Recurrent hemorrhages were observed in 5 (6.2%) of 89 patients who were fol-

lowed up for more than 6 months after the treatment. Judged by this incidence of relapses, hormonal therapy does not appear to be inferior to surgical procedures in the treatment of functional uterine bleeding.

Prognosis in Acute Renal Insufficiency Originated After Delivery. J. H. Thaysen, S. Gjørup and O. Munck. Ugeskr. læger **120**:899-905 (July 10) 1958 (In Danish) [Copenhagen].

The prognosis for patients with acute renal insufficiency depends partly on the nature of the basic disease and partly on the duration and degree of severity of the complicating uremia. Reports from dialysis centers in Denmark emphasize that the high lethality in patients with acute renal insufficiency is almost entirely to be ascribed to the basic disease which causes the renal insufficiency. The prognosis for uncomplicated renal insufficiency is relatively good, even with uremia of long standing. Report is given on 9 women with acute renal insufficiency post partum, admitted to date in the dialysis section of the medical division of the Rigshospital. The basic disorder was in most cases reversible. The prognosis in such cases depends almost wholly on the treatment of the uremia. One patient with bilateral renal cortical necrosis died; after 51 days of conservative and dialytic treatment no restitution of renal function had resulted. In several of the survivors the reduction of renal function was prolonged. Combined conservative and dialytic treatment has changed the prognosis for acute renal insufficiency. Further reduction of the mortality in patients with acute renal insufficiency must first of all depend on active treatment of the basic disease when it continues to dominate the picture and threatens life. Only hemodialysis affords the possibility of bringing the patients into such a condition that this treatment can be carried out. All patients with acute renal insufficiency, irrespective of the character of the basic disease, should be transferred to a dialysis section as soon as possible.

Listerosis in Mother and Child. O. Kranendonk. Nederl. tijdschr. geneesk. **102**:1202-1206 (June 21) 1958 (In Dutch) [Amsterdam].

The first-born child of a woman, who had felt "grippy" some weeks before delivery, appeared healthy until the 4th day of life. Then the infant refused to drink, an exanthem was observed, and the head was bent backward. Spinal puncture yielded fluid containing some erythrocytes, and some slender, gram-positive rods were observed. Colonies of a bacterial organism grew in a culture of the spinal fluid. Intraperitoneal injection of the culture into mice resulted in death of the animals after from 1 to 4 days, and focal necroses were seen in the livers of the mice. The strain of the injected organism could be cultured from the livers and the heart-blood of the animals. The organism was identified as Listeria monocytogenes. Studies on the mother revealed that she harbored L. monocytogenes in the vagina 10 days and 3 weeks after delivery. The strain isolated from the mother was serologically identical with that cultured from the spinal fluid of the newborn infant. It is suspected that the mother was infected by a pet dog which some weeks before delivery had had fever and a stiff neck, although its sickness was not bacteriologically studied. Literature reports are cited to prove that more attention is being paid to L. monocytogenes as a pathogenic agent in man and in animals.

Staphylococcal Infection in Mothers and Infants: Maternal Breast Abscesses and Antecedent Neonatal Sepsis. J. A. Monro and N. P. Markham. Lancet **2**:186-190 (July 26) 1958 [London].

Most epidemics and sporadic infections have been caused by antibiotic-resistant strains of staphylococci belonging to the phage-type 80/81, which are now firmly entrenched and widely distributed in New Zealand. Thirty-seven cases of maternal breast abscess developing in the weeks after childbirth and known to have followed confinement in maternity homes were investigated. Of the 37 patients, 31 required hospital admission for incision and drainage, and in 32 patients bacteriological investigations were carried out. Coagulase-positive staphylococci were obtained from 31 of the 32 patients investigated, 24 of the strains being identified as phage-type 80/81 and 21 exhibiting a characteristic antibiotic-sensitivity pattern. The time of onset in 23 of the 33 abscesses was between 2 and 4 weeks after confinement, although no relationship in time was discernible regarding the advent of or any change in lactation. A history of cracked nipples (14) in the mothers or infection (25) in the infant or both was forthcoming from 27 of 29 patients interrogated. Antibiotics given to 22 patients afforded them no relief, and in no case did antibiotics facilitate remission, once a mass was formed. Both breasts were affected in 5 patients, and 16 patients required incision on 2 or more occasions. While the strain of the organism from the abscess was isolated from the mother's nose on only 2 of 12 occasions, the "abscess strain" was carried by the infant in almost all the cases studied. This same strain was isolated from the breast milk in almost half of the patients examined. The incidence of staphylococcic skin lesions has been reduced from 11 to 6% since the introduction of new nursing techniques. No frank examples of umbilical sepsis were encountered. The proportion of nursing and other hospital staff personnel carrying coagulase-positive staphylococci varied between 22 and 48%, the proportion of penicillin-resistant carriers re-

maining at about 70%. Similar figures were obtained from the medical staff. The over-all maternal carrier rate of coagulase-positive staphylococci ranged from 30 to 36%; however, the incidence of penicillin-resistant strains among the mothers (35%) was half that among the nurses. No coagulase-positive staphylococci were isolated from the dust and air samples taken from the nurseries and theaters in one hospital, although in another older institution 9 of 43 specimens were positive, 2 being identified as phage-type 80/81. The authors conclude that a nursery may be "seeded" with staphylococci from a nasal carrier among the staff and that a nursery "reservoir" of staphylococci may persist by hand or air transfer from infant to infant.

The Indications for Conservative Therapy for Intraepithelial Carcinoma of the Uterine Cervix. J. S. Krieger and L. J. McCormack. Am. J. Obst. & Gynec. 76:312-320 (August) 1958 [St. Louis].

The authors report on clinical observations made between 1950 and 1957 at the Cleveland Clinic Hospital on 114 patients in whom the diagnosis of cervical carcinoma in situ had been established. The cervical smear was used for the clean, normal-appearing cervix, and the cervical smear and multiple biopsies were used for the abnormal cervix. Sixty-five of the 114 patients were first suspected of having carcinoma in situ from routine cervical smears; diagnosis was established in 28 patients by means of smear and biopsy; in 21 patients with a concomitant disease diagnosis of carcinoma in situ was made incidentally. Until late in 1951 the treatment for cervical intraepithelial carcinoma was total hysterectomy performed within 6 weeks after diagnosis by conization had been made. Since 1952 the treatment of choice, in the absence of other diseases that may require hysterectomy, has been radical conization. To assess the adequacy of the conization, it should be followed up by systematic cytological examination if the lesion is noninvasive in the conization specimen, if the cervix remains patent after conization, and if repeated smears remain negative. Hysterectomy is reserved for those patients in whom cervical smears remain positive after conization, the cervix closes and renders smears unreliable, or other major uterine disease is present. Radical conization was carried out in 65 of the 114 patients; in 30 conization followed by hysterectomy or trachelectomy was performed; in 10 hysterectomy was done after biopsy, and in 2 hysterectomy only was performed; 2 patients received radium therapy, and 5 were not treated after consultation. Of the 65 patients with radical conization, 4 were lost to follow-up, and 61 were followed for 6 months to 7 years; cervical smears have been negative repeatedly in all but 2 patients. Of the 30 patients who underwent hysterectomy or trachelectomy after the conization, 26 had no residual disease in the excised cervix, and 4 had evidence of persistent carcinoma in situ. The hysterectomy had been performed in 3 of the latter patients because of the evidence of unusually extensive disease in the conization specimen. These data suggest that hysterectomy is not a therapeutic necessity in treating cervical carcinoma in situ. Treatment can be individualized and is usually limited to radical conization with systematic cytological follow-up.

Occurrence and Significance of Free Tissue Fluid in the Female Mammary Gland. M. Ratzenhofer. Geburtsh. u. Frauenh. 18:893-906 (July) 1958 (In German) [Stuttgart, Germany].

Under physiological conditions, such as the menstrual cycle and particularly during pregnancy, the interlobular, collagenous, supportive tissue of the mammary gland contains microscopically demonstrable amounts of free interstitial fluid (tissue fluid) rich in protein. The amount of the fluid was found to be considerably increased to a macroscopically recognizable edema of the breast in women with painful swelling of the mammary glands, in those with mammary fibrosis, and in those with chronic fibrous mastopathy. Increased amounts of this interstitial fluid in the connective tissue were also observed in patients with cancer of the breast and associated fibrous mastopathy and particularly in women with obstruction of the lymph passages by cancerous growth. Chemical examination of the blood-free tissue fluid obtained from patients with such noninflammatory, benign or malignant, changes of the mammary gland revealed a surprisingly high protein content (on the average 4.5 to 5 Gm. per 100 cc.); the proportion of the protein fractions was about the same as that in the blood serum, but the albumin-globulin ratio was higher. The isoagglutinins and the electrolytes were the same as in the serum, although their concentration was slightly lower. These findings indicate that the tissue fluid originates from the blood serum.

The considerable accumulation of fluid in the connective tissue spaces of the mammary glands in pregnant women and in patients with certain types of disease of the breast is the result of increased permeability of the vascular walls; this, in turn, is probably caused either by the altered endocrine balance during gestation or by a hormone imbalance in patients with mastodynia and mastopathy, and primarily by hyperesterinism. The transient presence of large amounts of fluid rich in protein in the mammary tissue, observed during pregnancy and lactation, is probably related to the nutrition and function of the mammary glands whose activity is increased during these periods. The excessive accumulation of this extracellular fluid in patients with hormone imbalance and other disturbances is a pathological manifestation; its

persistence causes fibrosis and hyaline degeneration of the interstitial tissue by the transformation of globular proteins in fibrous proteins and by the synthesis of solid mucopolysaccharides. There were no qualitative differences in the composition of the tissue fluids obtained from patients with benign and malignant processes.

PEDIATRICS

Neonatal Varicella: A Case Report with Isolation of the Virus. R. M. Ehrlich, J. A. P. Turner and M. Clarke. J. Pediat. 53:139-147 (Aug.) 1958 [St. Louis].

Varicella during the newborn period is uncommon, only 16 cases having been reported in which the disease occurred during the first 10 days of life. The authors present the history of an infant in whom the rash appeared on the 7th day. This is the third reported infant with neonatal varicella, on whom a complete autopsy was done, and it is the 4th fatality among 17 reported cases. In all 4 of the fatal cases the disease had its onset more than 5 days after birth. The infants born with the rash or with an early onset of the rash survived. A possible explanation for this is that in the infant who develops lesions soon after birth the viremia occurred in the mother at an earlier date. This may allow antibodies to be formed and then to pass the placental barrier to the infant, resulting in a more attenuated form of the disease. At postmortem examination of the infant studied the characteristic lesions were demonstrated in most organs. Endothelial as well as epithelial cells were involved. The spread of the virus probably occurred via the blood stream. Two conclusions can be drawn from this case: 1. Neonatal varicella may be more severe than generally thought, with a mortality of 20% as shown by the literature. 2. The onset of varicella between 5 and 10 days after birth appears to be more severe than when the disease occurs at an earlier age.

Clinical Study of Oral Phenoxymethyl Penicillin and Parenteral Procaine Penicillin G: Comparative Study of Results in 1266 Children. A. A. Mintz, C. Bashaw and L. L. Hill. A. M. A. J. Dis. Child. 96:179-183 (Aug.) 1958 [Chicago].

The recent introduction into clinical medicine of phenoxymethyl penicillin (penicillin V) provided a penicillin that is virtually insoluble and thus stable in the acid pH range of the stomach but soluble and readily absorbable in the alkaline pH range of the intestine. Reports indicate that orally administered phenoxymethyl penicillin produces blood concentrations considerably higher than an orally administered dose of the salts of penicillin G and concentrations somewhat lower than an equivalent parenterally administered crystalline dose, although the blood levels obtained with orally administered phenoxymethyl penicillin are superior to the levels obtained with comparable doses of intramuscularly administered procaine penicillin G. The group studied included 2,132 children who were admitted to the pediatric clinic with the usual infectious diseases found among a large indigent population and of whom 1,266 (59%) returned on the last day for evaluation. The patients were subjected to either of the following regimens: (1) procaine penicillin G—children less than 1 year of age were given 300,000 units intramuscularly daily, while children over 1 year of age were given 600,000 units daily for a period of 5 days and (2) phenoxymethyl penicillin —125 mg. (200,000 units) was administered orally every 6 hours for 5 days. No differences were noted as to the status of the patients after the 2 types of penicillin therapy in regard to initial clinical diagnosis, bacterial organisms isolated prior to therapy, and white blood cell counts. No pneumococci were present on repeat culture regardless of the type of penicillin used. Beta-hemolytic streptococci were still present in 30% of the patients on the 5th day regardless of therapy but were not present after the 10th day. On repeat culture as many or more Staphylococcus organisms (Staph. pyogenes var. aureus) were present after therapy as were present before. There were no significant differences in the number of side-reactions with the 2 types of penicillin.

Kwashiorkor: Report of Four Cases from Louisiana. V. M. Henington, E. Caroe, V. Derbes and B. Kennedy. A. M. A. Arch. Dermat. 78:157-170 (Aug.) 1958 [Chicago].

The protein-deficiency disease of children, referred to as kwashiorkor, has been reported from every part of Africa and from China, India, Malaya, Indonesia, Fiji, and the Philippines. It has also been reported from Hungary and Italy, from the Caribbean Islands, and from various parts of Central and South America. The 4 children presented are believed to be the first cases of kwashiorkor reported in this country. All 4 were Negro girls, ranging in age from 20 months to 11 years. The 1st and 4th patients presented findings which are regarded as reasonably typical of kwashiorkor as it is observed in equatorial Africa, while the 2nd and 3rd patients presented milder forms of the disease. The 1st patient (11 years old) had continuous vomiting and diarrhea, with passage of semiformed stools containing undigested food, ascariasis, profound inanition, generalized edema associated with hypoproteinemia and anemia, enlargement of the liver, a reddish tinge to the hair at the ends, apathy and mental retardation, and scaly follicular skin changes over the chest. The 4th patient, a very much younger child (20 months),

also suffered from vomiting, ascariasis, loss of weight, generalized edema, weakness, and pronounced mental apathy. Her hair did not show a reddish tinge but was lighter, sparser, and dryer than usual Negroid hair. The 2nd and 3rd patients, sisters of the 1st, presented typical manifestations of the disease but in a milder (forme fruste) form. Inanition and apathy were conspicuous. The scaly rash present over the buttocks of the 3rd child seemed to be similar to the changes observed in the early stage of kwashiorkor. The 2nd patient had the most marked reddish tinge to her hair.

All 4 children have improved with an improved dietary regimen, though they are still below normal in weight and height, particularly the 1st child who is the oldest of the 4 patients. The 4th child has been under observation too short a time to permit conclusions, but she has improved greatly on a high-protein diet. Provision of food of high-protein and high-vitamin content by the Louisiana State Health Department has undoubtedly prevented a relapse of kwashiorkor in the first 3 of these patients. On the other hand, all the children, especially the younger ones, still eat dirt, and for this reason, plus their lack of cleanliness, intestinal parasitism still presents an unsolved problem. The authors believe that other patients in the United States have kwashiorkor, and they hope that this communication will call attention to the importance of recognizing and treating them.

Early Diagnostic Criteria of Congenital Hypothyroidism. G. H. Lowrey, R. H. Aster, E. A. Carr and others. A. M. A. J. Dis. Child. **96**:131-143 (Aug.) 1958 [Chicago].

A series of 49 cretinous patients, ranging in age from 12 months to 32 years, have been followed from 1 to 32 years. The average age at the time of diagnosis was 12 months. A survey of these patients, three-fourths of whom were female, has revealed that 54% had at least 3 prominent symptoms of their disease by the end of the first month of life and 75% by the end of the third month. For purposes of comparison, 100 normal infants were followed in the well-baby clinic for at least 6 months. The most commonly observed findings, in order of frequency, were lethargy, constipation, feeding problems which included slow feeding, choking, failure to gain weight, and lack of interest, umbilical hernia, and skin changes. Sluggishness of intestinal peristalsis was a quickly recognized characteristic of the hypothyroid patient, only 4 of the cretins in this study failing to manifest this difficulty. Respiratory distress associated with cyanosis appeared in 15 patients in the first months of life, 6 of the parents reporting cyanosis at some time during the first 24 hours after delivery and oxygen being administered to 3 of the cretins for periods exceeding 24 hours. Noisy respirations were not an uncommon complaint. Abnormal dryness of the skin was noted within the 1st month of life by one-third of the parents and within the 4th month by more than three-fourths. Thickening of the tongue to the point that it protruded from the mouth and interfered with respiration or feeding was noted in two-thirds of the infants in this series, the abnormality being observed for the most part prior to the 3rd month and always by the 5th month. Four of the patients were observed to have goiters either at birth or in early childhood. Umbilical hernia, which seldom developed later, was noted during the first week of life in two-thirds of the series. Not one of the infants had attained an expected or normal linear growth for his chronological age in comparison with tables of Stuart and Meredith. A hoarse or deep cry was noted in half of the patients, and loud or difficult breathing in a like number. The heart rate in 35% of the patients was 100 or below and was at this age indicative of true bradycardia. In 11 patients (55%) rectal temperatures persisted below 98 F (36.6 C) until therapy was instituted. Less frequently noted skin changes included pallor, 10; mottling and "coldness," 8; carotenemia ("yellow skin"), 4; and prolonged icterus neonatorum, 6. Alkaline phosphatase determinations gave results below normal in 11 patients, and after one year of age the cholesterol levels were significantly elevated in the majority of the untreated cretins. The only pertinent hematological finding was that of a moderate hypoplastic anemia in half of the patients. The evaluation of bone maturation was a valuable screening device, since every patient adequately examined by x-ray for "bone age" had easily measured retardation. The diagnosis of cretinism can usually be made, with the aid of a careful history, adequate physical examination, and a few laboratory procedures, by 3 months and certainly before 6 months of age.

Incontinentia Pigmenti (Bloch-Sulzberger's Disease). M. Lamy, R. Garcin, B. Duperrat and others. Arch. franç. pédiat. **15**:577-585 (No. 5) 1958 (In French) [Paris].

The authors report a case of incontinentia pigmenti in a female infant who at birth had 2 bullae filled with a clear fluid, one on the right hand and the other on the left leg. More bullae appeared during the following days. These lesions were very small but were associated with red papules, apparently pruriginous, varying in size from that of a millet seed to that of a lentil. At the age of 1 month the bullae had disappeared, but there was an eruption of papules of lichenoid type and occasionally verrucose, mainly on the extremities. This eruption became generalized, but the thighs and legs were particularly affected; the pattern of the eruption was definitely linear. The family history was entirely negative. Blood studies revealed a consider-

able eosinophilia on repeated examinations, varying from 23 to 32 per 100 cc. A skin biopsy was made and revealed the characteristic triad of bullae, eosinophilia, and dyskeratosis. Repeated bouts of the eruption occurred in the course of the following months, but with decreasing severity. The eosinophilia became less pronounced and was restored to normal (2 per 100 cc.) when the infant was 8 months old. At the age of 10 months the clinical picture again was changed, and the diagnosis of incontinentia pigmenti was made. The papular eruption was replaced by pigmentary spots of a chocolate-brown color, of spattered shape, and arranged in stripes, particularly at the sides of the thorax. The mucous membranes were not involved. The development of the infant's body, as well as her mental development, was normal. Ocular or nervous disturbances were not observed. There was only a slight delay in dentition. The skin of the infant was brittle and sensitive to sunshine.

The causation of incontinentia pigmenti is unknown. There is a general tendency to consider the condition as a congenital malformation of nevoid type. This concept is based on the appearance of the eruption at birth or during the first days of life, the occurrence of familial cases which may be rare but definite, suggesting a Mendelian dominant, and the frequent association with malformations of the eyes and the nervous system, suggesting a true congenital neuroectodermosis. Other concepts proposed include an infectious and an allergic origin. In agreement with most of the workers, the authors consider incontinentia pigmenti a dysembryoplasia, often associated with other congenital malformations, occasionally familial, the mechanism of which is unknown.

Lymphangioma of the Genitalia in Children. S. A. Gueukdjian. Pediatrics **22**:247-249 (Aug.) 1958 [Springfield, Ill.].

The author reports on a 3-year-old boy with a swelling of the penis and left groin which had been present recurrently since birth, without pain or ulceration. Exploration was carried out through a left inguinoscrotal extended incision. The subcutaneous tissues down to, but not including, muscle were found to be invaded by a network of multiple cysts containing lymph. The walls of the cysts were thin, glistening, and frail. The limits of the infiltrated area were well defined. En bloc excision was carried out. A polyethylene catheter was inserted subcutaneously, and the skin was closed with interrupted silk sutures. Continuous suction was maintained for 3 days, the catheter being gradually withdrawn every day. Antibiotics were given parenterally as prophylaxis. At subsequent examination as an outpatient, the boy was considered cured; there were no signs of lymphorrhea or recurrence, up to 1½ years after the operation. Microscopic examination of the operative specimen revealed cysts lined with a single layer of endothelium and surrounded by loose fibrofatty tissue. The diagnosis was lymphangioma. There was no evidence of malignancy. Lymphangioma is an uncommon benign neoplasm of the lymphatic system. If surgical and pediatric interest were directed to it, the condition would be diagnosed more often. Localization of these tumors in the region of the groin and external sex organs is unusual and presents diagnostic problems. Most of the cases occur in childhood. Treatment is by excision, but recurrences are to be feared.

Appendicitis in Childhood: A Study of 1,358 Cases. L. A. Longino, T. M. Holder and R. E. Gross. Pediatrics **22**:238-246 (Aug.) 1958 [Springfield, Ill.].

The author reports on 1,358 patients who were admitted to the surgical service of the Children's Hospital in Boston with acute appendicitis and were treated between July 1, 1944, and Jan. 1, 1957. Seven hundred forty-three patients (56%) were boys. Six hundred eleven (45%) had a ruptured appendix. Of these, 369 were less than 6 years of age, 231 were between the ages of 6 and 12 years, and 11 were over 12 years of age. The younger the child, the greater the likelihood of rupture. Only 1 patient, who was less than 2 years of age, died, a mortality rate of 0.07%. There have been no deaths in the last 12 years during which 1,309 patients were operated on. Patients with an unruptured appendix were hospitalized for less than 6 days, and those in whom the appendix had ruptured were hospitalized for about 12 days. Almost all the complications which were observed occurred in patients with a ruptured appendix. The most common complications were abscesses and other infections. Prompt appendectomy is the treatment for all children with appendicitis. Early diagnosis is of utmost importance, although in small children this may be difficult. The triad of abdominal pain, fever, and vomiting should be considered indicative of appendicitis until proved otherwise. To operate on these children with safety, adequate preoperative preparation and postoperative care are of greatest importance. The appendix was removed and the abdominal cavity drained in all the patients with ruptured appendix. Postoperative obstruction of the small intestine occurred in 45 patients; the obstruction occurred 5 to 10 days after the operation in 44, and 6 months after appendectomy and drainage in 1. Most of the immediate postoperative obstructions were managed successfully with a long intestinal tube.

The fact that nearly 50% of the patients had rupture of the appendix before the time of hospitalization is strong proof that diagnostic methods need to be improved. The early recognition of this disease would permit surgical intervention before rupture

and peritoneal soiling has occurred. The most important effort that can be made in this direction is to recommend 24 to 48 hours of observation in a hospital for any child in whom appendicitis is suspected. At little expense, this allows frequent checking by appropriate members of the resident or visiting staff of the hospital. If findings suggestive of inflammation of the appendix disappear, the child generally can be sent home the following day. For one in whom the abdominal findings become more impressive under observation, operation can be performed while there is still an opportunity to do so before rupture of the appendix has taken place.

Neurological Complications of Pertussis Immunization. J. M. Berg. Brit. M. J. 2:24-27 (July 5) 1958 [London].

The sequelae after active immunization against whooping cough have ranged from transient convulsions with complete recovery to gross crippling, mental retardation, and death. The author reports the case of an 8-month-old male child who received a first inoculation of 1 ml. of combined diphtheria-pertussis vaccine containing a plain suspension of 20,000 million Hemophilus pertussis bacilli and 25 Lf of fluid diphtheria formol toxoid. Within 48 hours convulsive episodes began. At 11 months of age the child was severely retarded mentally, and the administration of 16 mg. of phenobarbitone twice daily was required to control his convulsions. At 15 months grand mal episodes became associated with the original convulsive pattern, and it was found necessary to increase the phenobarbitone dosage to 1 Gm. At 3 years the child remained grossly mentally retarded, with no speech or understanding of speech, inability to do anything for himself, and an IQ of 23 on the Griffiths mental developmental scale.

The author has reviewed a total of 107 cases in the literature, from some 25 sources, pertaining to pertussis immunization. The age of inoculation ranged from 4 days to 3 years. In 28 children a pertussis vaccine alone was used, and in 28 a combined pertussis-diphtheria vaccine. No significant difference is accorded the use of either preparation, although there is general agreement that the pertussis antigen is responsible for the reported neurological sequelae. The dosage of H. pertussis bacilli ranged from 1.5 to 45,000 million with no particular tendency for reactions to be associated with the larger doses. In 61 instances a reaction occurred with the first injection, and although the data indicate that a reaction may occur with any injection, there is a decreasing likelihood of reaction to subsequent injection, provided that previous injections have not elicited some activity. The early onset of symptoms was characteristic, although not invariable, the greater majority of reactions occurring within 12 hours. Convulsions were an almost invariable and striking feature. Paralyses were reported in 19 of the 107 cases. Death occurred within 48 hours of inoculations in 8 cases, 7 of the deaths occurring within 24 hours. Additional features, other than the neurological, included diarrhea, vomiting, cyanosis, and hiccups. Complete recovery was reported in 41 patients (38%) and presumably occurred in at least 9 other instances. A total of 31 children (29%) were reported as having physical and/or mental signs of cerebral involvement 1 month to 5½ years after immunization. Follow-up revealed a mortality of 14% (15 of 107 children). Included among the various hypotheses advanced to account for the complications are: (1) sensitization phenomenon; (2) specific toxin or toxins produced by H. pertussis; (3) constitutional predisposition in affected children; (4) pyrogens contaminating vaccines; and (5) accidental intravenous injection of vaccine.

Persistence of Fetal Ductus Function After Birth: The Ductus Arteriosus as an Avenue of Escape. H. L. Abrams. Circulation 18:206-226 (Aug.) 1958 [New York].

The author reports on 9 infants, between the ages of 6 days and 9 months, with various congenital cardiac anomalies in whom the fetal veno-arterial flow through the ductus arteriosus persisted after birth. The conditions associated with persistence of fetal ductus function after birth included isolated patent ductus arteriosus with marked increase in pulmonary resistance, patent ductus arteriosus associated with congenital pulmonary disease, pulmonary vein atresia, mitral atresia, mitral stenosis, aortic atresia, interruption of the aortic arch, and preductal coarctation. In all these conditions, the pulmonary arteriolar resistance must be significantly elevated to permit flow into the descending thoracic aorta. Beyond this, the common denominator of the malformations, in which right-to-left flow through the ductus arteriosus persists after birth, is the presence of a site of obstruction to blood flow in the pulmonary vessels, left heart, or aorta at some point beyond the pulmonary origin of the ductus arteriosus but proximal to its aortic insertion. The ductus serves as an "avenue of escape" in most of these lesions; in no other way could blood leaving the right ventricle reach all or part of the systemic circulation without precipitating or increasing right or left heart failure.

That the ductus arteriosus, however, does not provide an effective method of sustaining life indefinitely in these circumstances is clear from the fact that 7 of the 9 infants died; the average duration of life was above 13 months, and 3 infants died before the age of 1 month. In one of the surviving patients, in whom surgery was not permitted, a state of balance consistent with life has apparently

been reached; this patient is still alive at the age of 4½ years. The other surviving patient, who had coarctation of the aorta, with a right-to-left shunt through a patent ductus arteriosus complicated by a ventricular septal defect, was operated on. Surgical closure of the ductus and excision of the coarctated segment were followed by improvement. Closure of the ventricular septal defect is contemplated after a period of stabilization. Increased resistance in the pulmonary vascular bed is reversible in some cases of coarctation associated with reversed flow through the distal part of the ductus. This may have significant implications for all lesions in which reversal of flow through the ductus is based on the primary increase in resistance beyond the pulmonary arteriolar bed. With improved techniques of open heart surgery, complete correction for all these anatomic malformations may be feasible, and it seems reasonable to suppose that closure of the ductus arteriosus, when normal anatomic channels elsewhere have been restored, need not necessarily be a hazard despite the obvious increase in pulmonary resistance.

Familial Thalassemia and Erythremic Myelosis. I. Olshin and A. Sawitsky. Pediatrics **22**:250-258 (Aug.) 1958 [Springfield, Ill.].

The authors report on a 10-year-old boy of Italian background who had been well until an attack of mumps followed by weakness, lassitude, and pallor. Two months later scleral icterus, enlarged liver and spleen, and tenderness over the sternum and long bones were noted. The findings of anemia, erythrocytosis, anisocytosis, poikilocytosis, target cells, and basophilic stippling in the patient and his parents, a shift of the saline fragility curves to the right in the parents, and anemia and erythrocytosis in a brother and a sister of the patient made it evident that the hereditary leptocytosis (thalassemia) trait was present in the family. Marked erythroid hyperplasia, however, was found in the patient's bone marrow, with many proerythroblasts and abnormal immature erythrocyte precursors. These findings were reflected in the patient's peripheral blood in which 100 nucleated erythrocytes were counted for every 100 leukocytes. The presence of atypical, primitive erythrocyte precursors in the marrow and peripheral blood and the late onset of symptoms in the patient made it unlikely that the disease was thalassemia but rather suggested a more malignant process, namely, malignant erythrocytosis (Guglielmo's disease).

Treatment of the patient's condition with cyanocobalamin (vitamin B_{12}), folic acid, and cortisone was ineffective. Monthly blood transfusions were required to maintain the concentration of hemoglobin at about 8 Gm. per 100 cc. Splenectomy was followed by transient improvement for the next 3 months. Myeloblastic proliferation then occurred in the bone marrow and in the peripheral blood. The myeloid phase was suppressed by the administration of mercaptopurine. Transfusions were continued as required. Twelve months after the onset of the disease, an area of nontender induration occurred in the right cheek. Six months later a biopsy of this mass revealed malignant reticulum cells interspersed with immature hematopoietic elements, which were considered characteristic of "erythroblastoma." Still 3 months later the patient sustained a mild injury of the left elbow, which was followed by hemarthrosis and subluxation of the joint and was complicated by an infection of the joint with Bacteroides subtilis. Intensive antibiotic therapy for several months was required to control the infection. Moniliasis of the mouth occurred and subsided after topical and systemic treatment with nystatin, but congestive cardiac failure, probably secondary to anemia and prolonged treatment with large doses of steroids, resulted in death.

Autopsy revealed erythroblastic infiltration of the bone marrow, liver, lungs, lymph nodes, and heart. Increased amount of hemosiderin was also observed. The gastrointestinal tract revealed areas of hemorrhagic necrosis of the submucosa and invasion of this tissue by leukemic cells, polymorphonuclear cells, and yeasts. There was evidence of severe degrees of systemic mycosis. In this patient with familial thalassemia a myeloproliferative disorder with bidirectional involvement occurred; the inherited red blood cell defect probably was the cause of the predominant expression of the disorder in the erythroid system. With a growing awareness of the hazards associated with prolonged steroid and antibiotic therapy, it became evident that many of the patient's clinical and pathological manifestations, such as the infection of the elbow joint, the monilial infection of the mouth, and the widespread systemic mycotic infiltrations revealed by autopsy, were secondary to these therapeutic agents rather than to the primary disease.

Rubella: Demonstration of Neutralizing Antibody in Gamma Globulin and Re-evaluation of the Rubella Problem. S. Krugman and R. Ward. New England J. Med. **259**:16-19 (July 3) 1958 [Boston].

Contradictory results reported about the efficacy of gamma globulin in the prevention of rubella induced the authors to investigate the presence of neutralizing antibody in ordinary gamma globulin, convalescent-phase rubella plasma, and gamma globulin prepared from plasma of patients convalescent from rubella. The serum, containing rubella virus taken from patients on the first day of rubella rash, was mixed with equal portions respectively of ordinary gamma globulin, of convalescent-phase rubella plasma, of convalescent-phase rubella gamma globulin, and of normal human serum. Each of the 4 mixtures was inocu-

lated into 4 comparable groups of 6 presumably susceptible children. The material was given intramuscularly in a dose of 1 ml. Five of 6 children who received rubella serum plus normal serum contracted typical rubella after incubation periods ranging from 15 to 21 days. One of 6 children receiving virus and ordinary gamma globulin acquired characteristic rubella on the 17th day. In the group receiving convalescent-phase plasma mixed with virus, rubella developed in 1 subject 14 days after inoculation. All 6 children who received the mixture of virus and convalescent-phase gamma globulin remained well. Thus, it appears that passive protection against rubella can best be achieved by early administration of large doses of gamma globulin. Future controlled field studies will have to define the precise dosage. In the meantime, gamma globulin in a dose of 0.15 to 0.20 ml. per pound of body weight appears to be indicated. It has been the practice to give 20 ml. intramuscularly to women exposed during pregnancy. If convalescent-phase rubella gamma globulin is available, 10 ml. given intramuscularly should be sufficient.

The authors also comment on recent prospective studies assessing the risk of fetal abnormality. Evidence suggests that the potential risk is increased approximately 6 times if rubella is acquired in the first trimester of pregnancy. The prevalence of congenital malformations has been estimated to be approximately 12%. Therefore, it is incumbent upon the physician to consider each case in the light of its individual merits. The deliberate exposure of young girls to rubella is recommended. One attack of this benign disease of childhood is generally followed by immunity. At the present time this procedure is the best method of preventing the serious effects of rubella in the offspring.

Myasthenia Gravis in Children. R. L. Sampayo and L. C. Stigol. Arch. argent. pediat. **29**:154-167 (April) 1958 (In Spanish) [Buenos Aires].

Myasthenia gravis in infants and children is more frequent than is generally assumed. A diagnosis is made by the results of the Prostigmin test, which consists of the intramuscular injection of neostigmine (Prostigmin) bromide in doses ranging from 0.07 to 0.1 mg. in newborn infants and of the subcutaneous injection of 0.5 mg. of the drug in children up to the age of 10 years. The myasthenic syndrome is observable in the newborn infants of mothers who are suffering from the disease, whether or not the mothers have received Prostigmin. Palpebral ptosis and disorders of deglutition appear during the first 48 hours after birth, and the infant is constantly moaning. On the administration of Prostigmin by mouth, the patient reacts immediately and favorably. After 15 days the treatment is discontinued and needs not be resumed. Both in infants and in children myasthenia gravis may start with acute symptoms and may be complicated by more or less serious bronchopulmonary diseases. The symptoms, which are similar to those observed in adults, consist mainly of fatigability and progressive paralysis of certain muscles, especially those of the face, lips, tongue, throat, and neck. There are no sensory disturbances. The cerebrospinal fluid is normal, and the patient remains completely alert to his environment.

The subjects of this report were 2 girls, aged 5 and 8 years. Ptosis appeared in both patients at the age of 2 years. It was bilateral in one case and unilateral in the other. In both patients it was total. One of the patients had been treated with Prostigmin but with dosage that the parents did not know. In both patients the Prostigmin test and Jolly's myoelectric test for myasthenia gravis gave positive results. Treatment has been given to only one of the patients. It consisted of the administration of pyridostigmine (Mestinon) bromide in doses of 60 mg. 3 times a day. All the symptoms of myasthenia, including palpebral ptosis, disappeared. The patient is now in a satisfactory state of general health.

The authors believe that pneumomediastinum as a diagnostic procedure for the presence of tumoral thymus is unnecessary and that thymectomy is ineffective in children. Thymectomy is a very serious operation, the results of which are no better than those obtained with medical treatment with Prostigmin.

Acquisition of Intestinal Protozoa and Helminths by Young Children in a Typical Village of Lower Egypt. R. E. Kuntz and D. K. Lawless. Am. J. Trop. Med. **7**:353-357 (July) 1958 [Baltimore].

The authors studied 81 children weekly for their intestinal fauna over a period of 16 weeks at Sindbis, a village representative of the delta area of lower Egypt. Of the 81 children, 23 were between the ages of 1 and 6 months, 30 were between the ages of 13 and 24 months, and 28 were between the ages of 26 and 47 months. The intestinal fauna of the youngest group was limited quantitatively and qualitatively, and only flagellate protozoa were detected. Examination of stool specimens obtained from the children between 13 and 24 months of age indicated that the period between 15 and 20 months was very important from the standpoint of general establishment of intestinal fauna in a child. Flagellates increased in number, amebas were detected, and the eggs of Ascaris, Enterobius, and Hymenolepis nana were passed with the feces. At the age of 16 to 18 months Entamoeba histolytica became established, the rate of infection increasing rapidly during the next 2 years. In the oldest age group, protozoan and helminth populations increased markedly, and none of the 28 children in this group escaped invasion by intestinal fauna.

A total of 9 species of protozoa and, in addition, both the large and the small races of E. histolytica and 6 different helminths were found in the latter age group by the time this study was terminated. Although Sindbis lies in an endemic area, neither of the 2 schistosomes common to Egypt were found.

Penicillin in the Treatment of Streptococcal Infections: A Comparison of Effectiveness of Five Different Oral and One Parenteral Form. B. B. Breese and F. A. Disney. New England J. Med. **259**:57-62 (July 10) 1958 [Boston].

The authors treated 611 children, between 1 and 17 years of age, who had infections due to beta-hemolytic streptococci, with 1 form of parenterally administered penicillin and 5 different preparations given orally in order to determine their effectiveness against streptococcic infections. Of the 611 patients, 122 received a total dose of 600,000 units of benzathine penicillin G, 237 were given a total dose of 8 million units of phenoxymethyl penicillin (penicillin V), 114 received a total dose of 8 million units of buffered potassium penicillin G, 66 were given a total dose of 7.5 million units of buffered potassium penicillin G and probenecid, and 72 received 5 million units of buffered potassium penicillin G and probenecid suspension. These children were observed for 2 months after the institution of therapy. No patient was included in the study who did not have a throat culture at least 11 days after the onset of therapy. Acute tonsillitis or pharyngitis was diagnosed in almost 70% of the patients; 19% were carriers; 5.4% had cervical adenitis and 4.7% scarlet fever. The remaining patients had infections, such as otitis media, sinusitis, and cellulitis. Uniformly good immediate results were obtained with all the preparations tested.

The ultimate effectiveness of these drugs, as judged by the cure rate at the end of 2 months, the relapse rate within 25 days, and the proportion of strongly positive cultures obtained from patients with relapses, indicated that a single intramuscular injection of 600,000 units of benzathine penicillin G was superior to the preparations given orally. The parenterally administered penicillin preparation may have the additional value of preventing some subsequent unrelated streptococcic infection. Among the orally administered drugs no single preparation was significantly superior to the others. The choice of which one to prescribe is incumbent on the physician. The skin reactions which were observed after probenecid had been used for more than a week were harmful, although not serious. Parenteral administration of penicillin is cheaper than the administration of oral preparations and is not associated with the problems encountered with the latter. Benzathine penicillin G given in a single dose of 600,000 units intramuscularly is the authors' first choice in the treatment of streptococcic infections in children. Its chief disadvantage lies in the painful local reactions frequently observed and the psychological trauma engendered by the use of a needle.

Therapeutically, but not prophylactically, the oral preparations used were almost as effective as the one administered parenterally. The choice of which oral drug to select should be based on factors other than effectiveness, since there is no evidence to indicate the therapeutic superiority of any one product. Since cost is often the most important factor, among the oral preparations tested, buffered potassium penicillin G in a dosage of 800,000 units daily for 10 days is the first choice for oral treatment of streptococcic infections in children.

OPHTHALMOLOGY

Metastatic Carcinoma of the Retina: Report of a Case and the Pathologic Findings. R. J. Kennedy, W. D. Rummel, J. L. McCarthy and J. B. Hazard. A. M. A. Arch. Ophth. **60**:12-18 (July) 1958 [Chicago].

Metastatic carcinoma of the eye, involving the retina alone, is an extremely rare lesion, only 2 cases having been previously reported. The authors report on a secondary carcinoma of the macula of the right eye, the primary site of which was the rectosigmoid. The patient underwent surgery for a grade 3 adenocarcinoma of the rectosigmoid. Ophthalmoscopic examination 3 months later revealed that the lesion in the macular region of the right eye, which had been previously diagnosed as metastatic carcinoma of the choroid with macular involvement, had enlarged, with new vessels coursing over it. Enucleation was done, and sections revealed a neoplasm involving the retina which was histologically similar to that found in the rectosigmoid.

Gross sections revealed a small discoid, grayish-white, nonpigmented lesion at the posterior pole, elevating the retina but not distending the choroid. The anterior segment and the posterior sections were within normal limits. The sections adjoining the nasal border of the lesion showed a pink-staining acellular fluid elevating the retina from the retinal pigment layer. Temporal to the latter section, the tumor mass involved the retina, which had lost its architecture, exhibiting necrosis and degeneration of the various layers and the adjoining subretinal space. The choroid was normal save for focal sites of perivascular inflammation and hyperemia in the region of the lesion. The neoplasm was formed of atypical stratified-columnar epithelial cells in small nests with lumens and separated by patches of necrotic tumor material. No tumor growths were found in the choroid, sclera, optic

nerve, or vitreous, and there were no implantation growths. The patient died within 3 months, possibly because of generalized metastases.

Audiometric Studies on Patients with Degeneratio Pigmentosa retinae. B. Alberth, A. Bálint and A. Kósa. Klin. Monatsbl. Augenh. 132:797-806 (No. 6) 1958 (In German) [Stuttgart, Germany].

Audiograms were obtained with the aid of an audiometer from 11 men and 6 women with retinitis pigmentosa, who were examined at the ophthalmological clinic of the University in Debrecen, Hungary. In 15 of the 17 patients the disease was acquired (autonomic), and in 2 it was primary (hereditary). Mild to severe degrees of hardness of hearing for the higher sounds were observed in all the patients. An additional selective loss of the power of hearing was observed at 4096 cps. These 2 characteristics suggested that the hardness of hearing originated in the nervous system. The impairment of hearing paralleled the narrowing of the visual field rather than the decrease of visual acuity. It was the authors' impression that the changes in visual acuity, which resulted from combined treatment of 10 patients with vitamins A, B_1, and C, liver, and various vasodilators and placenta implantations according to Filatow's technique, paralleled the changes in hearing in most of these patients. It was not possible to establish a precise relationship between the vision (visual field) of one eye and the hearing of the homolateral or contralateral ear. Lateralization, i. e., the possibility of a certain relationship between one eye and the contralateral ear, which has been suggested by some workers, remains an open question.

The fact that a loss of hearing was established in all the patients with pigmentary degeneration of the retina favors—in addition to many other reasons—the concept that the autonomic pigmentary degeneration of the retina is likewise neither an isolated disease of the eye nor the result of a local cause, but that it is rather closely connected with the central nervous system. Both the hereditary and the autonomic type of the disease may develop as concomitant manifestations resulting from a lesion of a central anatomic structure not yet identified.

THERAPEUTICS

The Use of Hydrocortisone in the Treatment of Tuberculous Meningitis. R. L. Cranny and V. C. Kelly. A. M. A. J. Dis. Child. 96:165-168 (Aug.) 1958 [Chicago].

The Reddy modification of the Reddy-Jenkins-Thorn technique was used to determine the levels of 17-hydroxycorticosteroids (17,21-dihydroxy-20-ketosteroids) in several samples of spinal fluid withdrawn 4 hours after the oral or the parenteral administration of hydrocortisone. Extremely small amounts of detectable Porter-Silber chromogens were present in the normal control spinal fluid samples. However, 17-hydroxycorticosteroids (17-OHCS) were present in all the samples from the patient with tuberculous meningitis after administration of hydrocortisone either orally, intramuscularly, or by both routes. They were also detected in 2 children without tuberculous meningitis 2 and 4 hours after the intravenous administration of hydrocortisone. A positive Porter-Silber reaction was not forthcoming after the administration of 100 mcg. of PAS and of isoniazid. In the single case cited, no evidence of spread of tuberculosis induced by hydrocortisone was noted. An interesting, though as yet unexplained, observation was the finding of a high concentration of 17-OHCS in the spinal fluid of a patient with tuberculous meningitis 2½ months after hydrocortisone therapy had been discontinued—a finding which has been attributed to either a continued release of steroids that had accumulated in the tissues or the increased permeability of the "blood-brain barrier" to steroids during the acute and convalescent stages of different diseases.

Clinical Studies on Tebamin. K. Tørning, K. A. Jensen and I. Kiaer. Acta tuberc. scandinav. 35:87-100 (No. 2) 1958 (In English) [Copenhagen].

It has been demonstrated that, when aminosalicylic acid is given in conjunction with isoniazid or streptomycin, the development of bacterial resistance to these 2 valuable drugs may be prevented for a long time. For that reason aminosalicylic acid today is indispensable in the chemotherapy of tuberculosis. Unfortunately, oral administration of aminosalicylic acid often entails such marked dyspeptic disturbances that long-term treatment becomes difficult, if not impossible. Furthermore, during ambulant chemotherapy there is always a possibility that unwise patients may stop taking the drug, without informing the physician, thereby exposing themselves to the serious risk of the development of chemoresistant tubercle bacilli. The authors for several years experimented with a derivative, the phenyl ester of aminosalicylic acid, known as Tebamin. The first preparation employed in these tests was micronized Tebamin in tablet form. The results of combined treatment with Tebamin tablets (5 Gm. 3 times daily) and isoniazid were promising, as far as prevention of the development of resistance was concerned. The level of free aminosalicylic acid in the blood was, however, rather low. Other Tebamin preparations were tried, and now for more than a year the authors have used Tebamin in the form of a powder, consisting of finely micronized Tebamin treated with a surface-active substance and mixed with an equal part of sucrose. A fine suspension is obtained when the

powder is carefully mixed with water or milk. After oral administration, some 80% is absorbed. Preliminary tests on healthy subjects and on patients have demonstrated that Tebamin is nontoxic and that it causes only negligible dyspeptic disturbances.

The main object of the studies described was to investigate the capacity of Tebamin to retard the development of resistance to isoniazid. For this study, 22 patients were selected and were treated daily with 4 mg. of isoniazid per kilogram of body weight in 3 divided doses, together with Tebamin in doses of 4 Gm. given 3 times a day after meals. With this treatment there was no increase in the resistance of tubercle bacilli to the 2 drugs, Tebamin and isoniazid. Furthermore, direct smear and culture of the sputum or culture from gastric lavage showed that all the patients had become free from tubercle bacilli, with the exception of one who was treated for 9 weeks only. The observation period, throughout which weekly examinations of the sputum or gastric lavage were made, was in 14 cases longer than 30 weeks; in 7 cases it was between 18 and 29 weeks; and in 1 case it was only 9 weeks. The studies proved that Tebamin is suitable for combined treatment with isoniazid. When this therapy is employed, only minimal dyspeptic disturbances arise, and the development of resistance of tubercle bacilli is prevented.

Nil nocere!: Deafness Caused by Intramuscular Administration of Neomycin. S. Körtge-Stöppler and G. Mittag. München. med. Wchnschr. **100:** 1189-1192 (Aug. 8) 1958 (In German) [Munich, Germany].

The authors report on 2 men and 2 women in whom severe disturbances of hearing resulted from the intramuscular administration of neomycin. Two of the patients were less than 30 years of age. The first patient had an inflammation of the urinary passages and was given 0.5 Gm. of neomycin intramuscularly twice a day for 5 days; the total dose of the drug administered was 5 Gm. On the 6th day she complained of tinnitus and difficulty of hearing. Administration of the drug was discontinued, but the disturbance became worse. The excitability of the apparatus concerned with maintaining equilibrium remained normal in both ears. The second patient who had chronic renal disease received the same neomycin therapy as the first patient and complained of tinnitus and poor hearing on the 9th day after the institution of the treatment; the difficulty of hearing increased within the following 11 days. The third patient had a recurrent furunculosis associated with cardiac disease for which he was treated with neomycin for 8 days; the total dose of the drug given intramuscularly was 7.5 Gm. Difficulty of hearing which began on the 11th day after the institution of neomycin therapy progressed to deafness; the excitability of the vestibular apparatus remained normal. The fourth patient had osteomyelitis and was treated with neomycin for 25 days; the total dose of the drug given intramuscularly was 12.5 Gm. Ten days after the cessation of treatment and on the 35th day after its institution, the patient complained for the first time of difficulty of hearing. The caloric excitability of the apparatus concerned with equilibrium remained normal in both ears.

These findings showed that the period elapsing from the institution of neomycin therapy to the onset of the disturbances of hearing was short. The difficulty of hearing increased after the withdrawal of the drug. Since there was evidence of a renal disorder (partly only mild) in all 4 patients, it has been emphasized again that intramuscular administration of neomycin is contraindicated in patients in whom renal disease is merely suspected.

Open Healing of Tuberculous Cavities: Results in 40 Patients Treated Conservatively. T. M. Wilson, L. Doyle and M. P. Gardiner. Brit. M. J. **2:**87-90 (July 12) 1958 [London].

The authors report on their experience with indefinite prolonged chemotherapy in the treatment of 40 patients with advanced pulmonary tuberculosis with persistent cavitation, who had been observed for periods ranging from 1½ to 5 years. Thirty-seven of the patients had been adjudged by virtue of age, advanced disease, or poor respiratory function as unsuitable for surgery, the remaining 3 patients having refused surgery. All the patients were sputum positive; 35 had received no treatment, and 5 had had previous chemotherapy with drug combinations considered unlikely to produce resistant organisms. Thirty-two of the patients received a triple drug regimen—streptomycin, PAS, and isoniazid—during the first year of treatment. The other 8 patients received varying drug combinations because of inability to tolerate PAS, partial nerve deafness, or allergic reaction to PAS. Only one of the patients did not continue to take antituberculosis drugs.

All the patients showed marked clinical and roentgenologic improvement, which usually continued into the second or third year of treatment. Tomograms showed marked resolution of disease, although multiple cavities persisted in 28 patients. Thin-walled, cyst-like cavities persisted in 25 patients; the residual cavities were apparently thick-walled in 12; and in 3 both varieties persisted. The rate of sputum conversion was rapid; 37 patients became sputum negative within 6 months and 2 during the 7th and 9th month; the last patient remained intermittently positive for 15 months. One other patient produced a solitary positive sputum culture during the third year of observation.

Chemotherapy of Tuberculosis: III. Verazide in the Treatment of Pulmonary Tuberculosis. S. D. Rubbo, L. C. Rouch, J. B. Egan and others. Am. Rev. Tuberc. 78:251-258 (Aug.) 1958 [New York].

The authors conducted a clinical trial of 3,4-dimethoxybenzal isonicotinylhydrazone (Verazide) in 3 hospitals in Australia, in which the response in 2 groups of patients with pulmonary tuberculosis was studied for 3 months. One group of 79 patients received Verazide and streptomycin, and a control group of 75 patients was given isoniazid and streptomycin. Verazide was given in a dose equivalent to 20 mg. per kilogram of body weight by mouth as enteric-coated tablets in divided doses twice daily after meals. Sixty-four of the 75 control patients were given 8 mg. of isoniazid per kilogram of body weight daily in 2 divided doses, and 11 received 300 mg. of isoniazid daily irrespective of their weight. All the patients received 1 Gm. of streptomycin, either on alternate days for the entire trial period or daily for 6 weeks and thereafter 3 times a week. The results, assessed on clinical, roentgenographic, and bacteriological criteria, showed that no difference in effectiveness could be seen between Verazide and isoniazid. However, Verazide, when given in uncoated tablets, caused toxic reactions, such as drowsiness, slurred speech, and occasionally blurred vision and nausea. These manifestations of intoxication of the central nervous system were not observed with isoniazid; they did not occur when Verazide was administered in enteric-coated tablets. These toxic effects of Verazide were attributed to the rapid absorption of veratric aldehyde released during partial acid hydrolysis of Verazide in the gastric juice. On the evidence available, no chemotherapeutic or pharmacological advantage can be claimed for Verazide, when compared with isoniazid, for the treatment of pulmonary tuberculosis.

Oral Treatment of Diabetes: Trial of Phenylethyldiguanide (D. B. I.). G. H. Hall, M. F. Crowley and A. Bloom. Brit. M. J. 2:71-74 (July 12) 1958 [London].

In the course of study to determine the effectiveness of phenylethyldiguanide (D. B. I.) as a hypoglycemic agent in diabetes of all grades of severity, to gauge its side-effects, and to compare its mode of action with that of insulin and tolbutamide, 40 diabetic patients were admitted to the wards. The subjects ranged in age from 18 to 78 years, with a mean average of 57 years. A significant fall in blood sugar levels was observed in 24 of the 40 patients in response to a single 150-mg. dose of D. B. I. The response began to be apparent at 4 hours and reached its maximum at 6. Although there was no significant change in the blood sugar levels during the period of dietary restriction alone, administration of D. B. I. led to a progressive fall in the mean blood sugars, the lowest level being attained by the 6th day of treatment. The urinary output of sugar reflected the blood sugar levels, and there was no evidence of an altered renal threshold. The 5 patients whose life depended on the administration of insulin developed ketosis very rapidly when insulin was withdrawn; their condition was not alleviated by the administration of D. B. I., although there was a small fall in the blood sugar level. In the remaining 35 patients only occasional positive "acetests" were recorded prior to treatment. After the administration of D. B. I. 11 of the 35 exhibited intermittent acetonuria of greater frequency and concentration than prior to treatment, although normoglycemia and aglycosuria prevailed. No effect of D. B. I. could be demonstrated on either plasma amino-acid nitrogen or serum inorganic phosphorus values. An inverse relationship was found to exist regarding the severity of diabetes and the response to D. B. I., patients with milder or moderately severe diabetes showing a fall in blood sugar level in response to the administration of D. B. I. Of the 14 newly diagnosed diabetics, 12 exhibited a good hypoglycemic response to D. B. I., and 5 of these did not have a relapse when D. B. I. was withdrawn. Of the patients with diabetes of long standing, 17 showed some hypoglycemic response, but none could subsequently be managed by diet alone, the impression being that D. B. I. was more effective in diabetes of recent onset. No fewer than 26 of the 40 patients developed gastrointestinal symptoms while receiving the drug; these symptoms abated upon discontinuance of the therapy. In 2 patients in whom tolbutamide had been employed unsuccessfully, D. B. I. was effective in lowering the blood sugar level. In 3 other patients in whom D. B. I. had produced normoglycemia and in whom treatment was discontinued because of nausea and vomiting, tolbutamide was slower and less effective in reducing the blood sugar value. It was impossible, as previously planned in 25 of the 40 patients, to administer D. B. I. for 6 weeks because of unpleasant side-effects or because an adequate fall in blood sugar level had not been realized. Six of the remaining 15 patients are still receiving D. B. I., and their condition is satisfactorily controlled.

Treatment of Acute Leukemia in Adults with Massive Doses of Prednisone and Prednisolone. N. B. Granville, F. Rubio Jr., A. Unugur and others. New England J. Med. 259:207-213 (July 31) 1958 [Boston].

The authors report on 20 consecutive cases of acute leukemia in adults treated with massive doses of prednisone. The first 10 patients received 1,000 mg. per day; the second 10 patients received 250 mg. per day. Prednisone and prednisolone were

used interchangeably and were given orally in doses of either 250 mg. every 6 hours or 125 mg. every 12 hours for a period of 2 weeks, after which time the dosage was carefully reduced to a maintenance dosage of 5 to 50 mg. per day. Only 3 of the patients treated with 1,000 mg. of prednisone per day were able to tolerate the medication for the entire 2-week period, the drug being withdrawn in 5 cases because of undesirable side-effects; 2 patients died in less than a week after the institution of therapy. The 250-mg.-per-day regimen was better tolerated, 9 out of 10 patients receiving the full course for 2 weeks. Three complete remissions (hematological, clinical, and bone marrow) and 1 partial remission occurred in the 1,000-mg. group and 2 complete remissions and 1 partial remission in the 250-mg. group. Remarkable symptomatic improvement was evident within 24 to 48 hours of treatment in most patients, the outstanding changes including the development of a striking sense of well-being, a marked increase in appetite, and, objectively, defervescence and decreased bleeding. Since corticosteroids or corticotropin (ACTH) had been employed prior to massive prednisone therapy in 2 instances and since a short course of mercaptopurine therapy had been given to 3 patients in the 1,000-mg. group in whom complete remission was noted, the value of prednisone could not be fully assessed. No previous therapy was noted in the 250-mg. group; however, the single clear-cut remission appeared only after a brief course of mercaptopurine therapy. Five of the patients in the 1,000-mg. group had an undesirable side-effect—namely, the appearance of an agitated depression bordering on frank psychosis—which did not occur in any of the patients in the 250-mg. group. In the instances in which relapse occurred, it was not possible to induce a second remission with massive prednisone therapy either singly or in combination with mercaptopurine. Although the percentage of remissions (25%) cannot be considered very striking, it does compare favorably with other therapeutic methods. The therapy with massive doses of prednisone appeared to be at least as effective as that with mercaptopurine, and in the 250-mg. dosage it seemed least injurious.

Hemodialysis: Technique, Effect and Indications. S. Gjørup, O. Munck and J. H. Thaysen. Ugesk. læger 120:893-897 (July 10) 1958 (In Danish) [Copenhagen].

Hemodialysis is regarded as a valuable and at times indispensable means of treatment of grave acute renal insufficiency. Conservative treatment is of fundamental importance in all cases independently of their duration and is not made superfluous by hemodialysis. In recent years it has become the practice to dialyze early in the course of uremia, and it is recommended that patients with acute renal insufficiency be transferred to a special dialysis section, at the latest 3 days after the onset of uremia. The dialyses, carried out to date, have shown that the treatment is tolerated surprisingly well even by extremely ill and older arteriosclerotic patients. If there is an acute reversible renal disease of such severity that hemodialysis is indicated, contraindications will rarely be absolute. In more recent dialysis of patients with hypertension, the blood pressure has been regulated by hypotensive substances. In patients with grave uremia, dialysis is performed in spite of bleeding from mucous membranes. The uremic changes in the mucous membranes disappear to a great extent after one dialysis, so that possible repeated treatment is tolerated without complications of this kind. The main indication for hemodialysis is wholly or partly reversible renal insufficiency of acute onset, especially shock kidney. There seems now to be agreement that, other things being equal, frequent dialyses to prevent grave, long-continued uremia lead to fewer complications both during the dialyses and during the continued convalescence.

Treatment of Cancer of the Prostate with "Depot" Estrogens. D. Salsano and M. Alpi. Minerva med. 49:2367-2370 (June 13) 1958 (In Italian) [Turin, Italy].

Estradiol valerate was administered by injection to 14 patients with cancer of the prostate, 5 of whom had not previously received any chemotherapy. The drug was administered at varying dosages for a period of from 3 to 8 months. The most efficacious dosage consisted of 20 mg. given every 10 days. However, in some instances a dosage of 10 mg. given every 7 days was sufficient. Subjective improvement in those patients who had not previously received any chemotherapy became perceptible 3 or 4 days after the onset of chemotherapy. There was also an improvement, although to a lesser extent, in the other patients. Subjective improvement affected the state of well-being, there being a decrease in pain in joints and of nerves, daily and nightly pollakiuria, tenesmus, and dysuria. Objective changes consisted in change of the complexion from pale to pinkish, gain in body weight, and appearance of gynecomastia. Vesical residuum, if present, decreased or disappeared after a month of drug treatment. At the beginning of chemotherapy, estradiol valerate affected only insignificantly the morphologic characteristics of the neoplastic lesion of the prostate, but in 7 patients who received more than 250 mg. of the drug the cancerous mass changed in consistency from a hard to a fibrinous tissue without any change in the total size of the prostate. Chemotherapy benefited for 5 months one patient who had cancer of the prostate in an advanced stage, accompanied by

bone metastases; afterward the condition of this patient deteriorated. The tolerance of the patients to the drug was good and, in the opinion of the authors, was superior to all other preparations of estrogens. It is suggested that the interval between 2 succeeding administrations of the drug be shortened from 10 to 7 days for large doses (20 mg.) and from 7 to 5 days for small doses (10 mg.), respectively, whenever the original symptoms relapse.

Intraperitoneal Neomycin in the Treatment of Acute Bacterial Peritonitis. H. G. Greene. Surg. Gynec. & Obst. 107:169-172 (Aug.) 1958 [Chicago].

Twenty of the group of 1,529 patients subjected to laparotomy developed acute bacterial peritonitis of such severity that the usual antibiotics were considered inadequate, and the patients were, therefore, given neomycin intraperitoneally. The patients, 13 of whom were male, ranged in age from 5 to 91 years, with a median age of 56 years. Nine had perforated appendixes; 6 had perforations of other viscera; and 5 had other lesions. No toxic effects of the drug were noted. Seven deaths (35%) occurred, 6 of the patients succumbing from causes other than peritonitis. The median hospital stay was 3 weeks. Sixteen patients suffered postoperative fever beyond the first 3 hospital days, the longest febrile course lasting 34 days and the median being 9 days. Six of the 13 survivors developed postoperative complications, 4 of them having wound abscesses, 1 having a pelvic abscess, and 1 a dehiscent abdominal wound. The original peritoneal culture showed no growth in 3 patients. In 5 patients a bacterial species was present; 8 patients had 2 species, and 4 had 3. The most common pathogens were those of the coli-aerogenes group which were present in 13 patients, followed closely by the streptococci of the viridans groups which were present in 7. In view of the innocuousness of this type of therapy and of the low mortality rate (5%) from infection, neomycin administered intraperitoneally in moderate-sized, divided doses is recommended as an adjunct to surgery for patients with severe acute bacterial peritonitis.

PATHOLOGY

A Comparison of Results Obtained from Transplantation and Replantation Experiments Using Syrian Hamster Teeth. H. I. Myers and V. D. Flanagan. Anat. Rec. 130:497-507 (March) 1958 [Philadelphia].

The authors performed transplantation and replantation experiments in 30-day-old Syrian hamsters which were anesthesized with intraperitoneally injected pentobarbital. The 3 molar teeth in these animals were fully erupted, and the roots were essentially fully formed. Bilateral mandibular second molars were extracted and replaced immediately in the socket in 15 animals. Sixteen litter-mate animals were used for the transplantation experiments. In each case, bilateral mandibular second molars of animal A were extracted and placed in sterile sodium chloride solution. Then bilateral second molars of animal B were extracted and also placed in sterile sodium chloride solution. The respective teeth of animal A were then placed in the sockets of animal B, and the teeth of animal B were placed in the sockets of animal A. These paired animals were kept in the same cage. The animals in each case were awake shortly after the surgical procedure and were quite alert within 1 hour. After 30 days the animals were killed; the mandibles were removed and placed in 10% formalin for 2 weeks. The tissues were electrolytically decalcified, paraffin embedded, and cut; every 10th section was mounted and stained with hematoxylin and eosin.

The success of the experiments was judged by the extent of the viability of the pulp, degree of attachment of the peridental membrane, amount of migration of the epithelial attachment apically, and extent of root resorption. Pulp, epithelium, and peridental membrane tissues proved to have the inherent capacity for complete regrowth. The pulpal regrowth occurred with greater difficulty than the regrowth of the other elements. Since regrowth occurred as well in the transplantation experiments as in the replantation experiments, no evidence of tissue incompatibility was noted. It would seem, therefore, that it is just as feasible to transfer a tooth from one hamster to another as it is to replant a tooth in the same hamster.

Tuberculosis Antibodies in Patients with Boeck's Sarcoid. W. Müller, K. Wurm and H. Reindell. Beitr. Klin. Tuberk. 118:229-243 (No. 4) 1958 (In German) [Berlin].

The authors performed hemagglutination and hemolytic modification tests for tuberculosis antibodies, according to Middlebrook and Dubos' technique, on serums obtained from 111 patients with sarcoidosis, from 60 patients with active pulmonary tuberculosis, from 28 patients with tuberculosis of lymph nodes, and from 50 normal persons. Tuberculosis antibodies were detected significantly more frequently in the serums obtained from patients with sarcoidosis than in those obtained from normal persons. Tuberculosis antibodies were detected less frequently in the serums of patients with sarcoidosis than in those of patients with pulmonary tuberculosis and tuberculosis of lymph nodes. No relationship between the occurrence of tuberculosis antibodies in the serums of patients with sarcoidosis and the stage of the dis-

ease, its activity, course, and duration, could be observed. Nor was any unequivocal parallelism between tuberculin sensitivity of the skin and the occurrence of serologically detectable circulating tuberculosis antibodies found. There was no relationship between the changes in the serum protein levels (such as increases in alpha and gamma globulin contents) in the serums of patients with sarcoidosis and the occurrence of tuberculosis antibodies in these serums.

The increased occurrence of tuberculosis antibodies in the serums of patients with sarcoidosis may be considered the result of a reaction to Mycobacterium tuberculosis. The serologic findings, therefore, seem to support the concept of tuberculous causation of sarcoidosis. An attempt was made to interpret the phenomenon of a weak or absent skin reaction of patients with sarcoidosis to tuberculin as a genuine dissociation between the cell-bound tuberculosis autibodies, which are responsible for the skin reaction, and the circulating antibodies, the presence of which has been demonstrated serologically. The reduced content of cell-bound antibodies in the skin is an immunological defect, which depends on a disturbance either of the formation or of the transportation of the cell-bound tuberculosis antibodies, while the formation of the circulating antibodies may be normal or increased.

RADIOLOGY

Interstitial Irradiation of the Pituitary Body With Yttrium 90: Indications, Technique, and Results. A. M. Dogliotti and A. Ruffo. Minerva med. 49: 2383-2389 (June 16) 1958 (In Italian) [Turin, Italy].

Destruction of the pituitary body by interstitial irradiation with radioyttrium (Y^{90}) was carried out in the treatment of 43 patients with advanced neoplastic disease. In 22 the diagnosis was carcinoma of the breast. The treatment consisted in implanting 3 small rods of Y^{90} through the left nostril into the pituitary body. There was no operative mortality, but there was one postoperative death attributed to meningitis. Autopsy on 3 patients revealed that the extent of destruction around the Y^{90} rods reached an area of from 3 to 4 mm. It is probable that Y^{90} permanently inhibited the function of the nonnecrotic cells. During the 30 days immediately after the operation, general improvement (decrease in or disappearance of pain, restoration of appetite, and gain in body weight) was evident in about 16 patients with mammary carcinoma (75%), and local improvement in the neoplastic lesion was found in about 10 patients with mammary carcinoma (45%). These improvements persisted on the average for 6 months, but no longer than 12 months.

Destruction of the pituitary body with Y^{90} seemed to have affected the malignant growth, other than carcinoma of the breast, in only 2 of 15 patients (14%). However, this procedure brought about subjective improvement in a patient with adenoma of the pituitary. The attempt to reduce the thyrotropic activity of the pituitary with Y^{90} in 2 patients with exophthalmos was crowned with such remarkable success that the authors recommended the procedure for refractory cases of the disease. Clinical improvement in one patient still persisted a year after the treatment with Y^{90}. The opinion of the authors is that a discriminating application of the interstitial irradiation of the pituitary body with Y^{90} is a useful procedure for the management of certain types of neoplasms, particularly those at the initial phase of growth, which are related to the pituitary body.

ANESTHESIA

Anesthetic Problems in Cardiopulmonary Bypass for Open Heart Surgery: Experiences with 200 Patients. A. S. Keats, Y. Kurosu, J. Telford and D. A. Cooley. Anesthesiology 19:501-514 (July-Aug.) 1958 [Philadelphia].

The authors review anesthetic problems in the management of 200 patients who underwent cardiopulmonary bypass for intracardiac surgery. This group included 102 patients with ventricular septal defects, 28 with atrial septal defects, and 18 with tetralogy of Fallot; the others had such defects as atrioventricularis communis, transposition of the great vessels, and various forms of aortic or pulmonary stenosis. The authors used bubble-type oxygenators with low-flow perfusion in all their patients. The perfusion rate for each kilogram of body weight per minute was 35 cc. for adults, 40 to 50 cc. for children, and 50 cc. for infants. In the first 60 patients, coronary artery perfusion was permitted continuously during bypass, and on rare occasions coronary blood was returned to the pump. In the next 73 patients, asystole of the heart during perfusion was accomplished by cross clamping the aorta and injecting potassium citrate solution into the proximal part of the aorta and coronary system. In the last 67 patients the proximal part of the aorta was clamped without chemical arrest of the heart and the clamp released intermittently to allow coronary blood flow.

Serious arrhythmias from extensive manipulations of the heart were minimized by the use of light general anesthesia. Hyperventilation was deliberately used to provide a high-tension tissue store of oxygen by nitrogen washout and a respiratory alkalosis which compensated for the mild metabolic acidosis produced by low-flow perfusion. It was not found necessary to add any anesthetic agent or carbon dioxide to the oxygenator during

cardiopulmonary bypass. Curare was administered prior to bypass to eliminate striated muscle contraction and to minimize metabolic acidosis. Its use with complete collapse of the lungs provided ideal operating conditions and had no deleterious effects. For blood replacement, fresh citrated blood was used for transfusion throughout the procedure in small children; in larger children and adults, stored citrated blood was used before bypass and fresh blood after bypass. Most patients were hypothermic after bypass; these patients were slowly rewarmed in the recovery room by a heating blanket. Ventricular fibrillation occurred in 33 patients during or immediately after bypass. It was most frequent after the use of potassium citrate to produce cardiac asystole. Twenty-one of the 33 patients with ventricular fibrillation were successfully defibrillated. A significant heart block occurred in 11 patients, presumably from sutures placed through the conduction bundle. If an adequate blood pressure could be maintained at the slow heart rate, usually no ill-effects ensued. The use of a mechanical pacemaker was not successful. A tracheotomy was performed at the end of the operation when large amounts of blood were removed through the endotracheal tube. Usually bloody secretions in the trachea were the results of pulmonary edema, but at times trauma from extensive retraction of the lungs was a causative factor. Tracheotomy facilitated removal of secretions and provided proper ventilation of the lungs.

There were 45 deaths in this series of 200 patients, a hospital mortality of 22.5%. Nineteen of the deaths occurred in the 40 infants under 1 year of age. This high death rate was chiefly the result of the severe heart disease. Over 90% of the deaths occurred in either the operating or the recovery rooms or within the first 3 days after operation.

PHYSIOLOGY

The Gastroesophageal Mechanism: II. Further Experimental Studies in the Dog. J. H. Meiss, J. H. Grindlay and F. H. Ellis Jr. J. Thoracic Surg. **36:** 156-165 (Aug.) 1958 [St. Louis].

In the first of 4 groups of mongrel dogs studied in an attempt to determine the nature of the mechanism responsible for gastroesophageal continence, the esophagogastric junction was removed and the esophagogastric anastomosis made in several ways. In the second group the acute esophagogastric angle was eliminated by resection of the fundus or by division of the stomach below the junction and subsequent anastomosis of the upper rim to the fundus. The animals in group 3 underwent formation of a partial thoracic stomach. The mucosal rosette was eliminated in animals of group 4, in addition to the elimination of the acute esophagogastric angle and the diaphragmatic pinchcock. Esophagitis developed in all the animals in the first group, indicating that an acute esophagogastric angle and the diaphragmatic pinchcock cannot prevent esophagitis after removal of the esophagogastric junction. Esophagitis did not develop in any of the animals in the second group; therefore, an acute esophagogastric angle is not necessary to prevent reflux esophagitis in dogs. The results of studies in the third group of dogs revealed that the diaphragmatic pinchcock is not an essential mechanism for the prevention of reflux esophagitis. Esophagitis did not develop in any of the dogs in the fourth group in whom the mucosal rosette was eliminated, in addition to the elimination of the acute esophagogastric angle and the diaphragmatic pinchcock. This left the presence of an intrinsic sphincter mechanism in the region of the esophagogastric junction as the only possible mechanism which could have prevented esophagitis.

PUBLIC HEALTH

Epidemic Virus Meningitis Due to ECHO 9 Virus in Newfoundland. J. W. Davies, A. McDermott and D. Severs. Canad. M. A. J. **79:**162-167 (Aug. 1) 1958 [Toronto].

In recent years there have been numerous reports of epidemic meningitis due to virus infection in which a rubelliform type of rash has been present in a large percentage of the cases. During 1957 a total of 44 patients with aseptic meningitis of this type were admitted to the Isolation Hospital in St. John's, Nfld., slightly more than one-third of the total admissions occurring during the month of August. The highest incidence (40.9%) occurred in the 5-to-9-year age group, the disease affecting the males predominantly in a ratio of 1.5 males to 1 female. In the 20-and-over age group this ratio was reversed, females predominating 5 to 1. A pronounced feature of this epidemic was the high attack rate—the secondary attack rate was slightly in excess of 50%—among family contacts, nearly one-third of the adults in contact with a patient at home being affected. The high proportion of positive viral isolations from throat washings, as compared with fecal isolations, suggests that droplet infection is the more important mode of spread.

Inasmuch as poliomyelitis and Coxsackie virus infections were absent in the population at this time, the clinical picture of enteric cytopathogenic human orphan (ECHO), type 9, virus infection appeared to conform with the following pattern: (1) history of biphasic illness, (2) highly contagious type of illness with a high attack rate among families, (3) typical exanthem, (4) two-phase temperature plot, (5) moderate pleocytosis and normal chemical findings in spinal fluid, and (6) leukopenia with relative lymphocytosis. Pathological material from 36 pa-

tients suspected of virus infection which was submitted for examination yielded virus on human amnion or monkey-kidney cell tissue culture in 17 cases. The virus was isolated from 13 of 28 specimens of spinal fluid, from 12 of 34 throat cultures, and from 5 of 28 rectal swabs or stools. The illness commenced generally with prodromal symptoms of anorexia, fever, chills, generalized muscular aches and pains, drowsiness, and headache.

Observations on the Potency and Safety of Poliomyelitis Vaccine (Salk Type) Currently Used. K. Sunada, R. K. Gerloff, D. Brock and others. A. M. A. J. Dis. Child. 96:125-130 (Aug.) 1958 [Chicago].

A total of 605 children, ranging in age from 5 to 15 years and residing in widely separated areas of Idaho, were given poliomyelitis vaccine, 143 uninoculated children serving as control subjects. Each child received 3 intramuscular doses; the first 2 injections were given in the spring and early summer of 1956, the second injection 1 month after the first, and the third injection was given 7 months after the second. The injection of the lots of vaccine used in this study was not accompanied by any illness suggestive of poliomyelitis in either the vaccinated children or their contacts. In the control children, natural infection and a concommitant increase in the antibody titer from 1:8 to 1:64 were evident in only one child in the early stages of the experiment and were impossible to calculate at a later date as many of the controls requested vaccination.

When type 1 antibody was present alone in the preinjection serum, type 2 antibody appeared in 94% of the children after the first injection. A similar response (72% conversion to type 2) was forthcoming when type 3 antibody was present in the preinjection serum. When antibodies against types 1 and 2 were present, type 3 antibody appeared in a higher percentage of children (50%) than when types 1 and 2 were present singly (13 to 22%). These differences still persisted after inoculation (86% as compared with 51 to 67%). In the event that antibody types 1 and 3 or types 2 and 3 were present in the preinjection serum, all 3 types generally appeared after only one injection. After one dose of vaccine, type 2 antibody appeared in the serums of 20% of those children who did not demonstrate antibodies in the serums prior to vaccination, types 1 and 3 being present in minimal amounts (7 and 4%). After 3 injections, 73 and 29% of the children showed antibody types 1 and 3, and practically all (99%) had type 2. While type 2 antibody resulting from natural exposure had a marked influence on the development of heterotype antibody after vaccination, type 2 antibody resulting solely from vaccination did not exert a comparable influence. The difference in the heterotypical response which did occur in children possessing type 2 antibody, as compared with those lacking this antibody, reflected in all probability not a true cross antigenic effect but rather a difference in the innate ability of the individual child to produce said antibodies.

In general, the data revealed that the 3 components of the poliomyelitis vaccine acted as specific entities and that they had little, if any, antigenic relationship to one another, the final development of an antibody to any one type of antigen resulting from a cumulative effect of that type of antigen rather than from a cross effect between types. A further dose given 3 months after the preceding one to 39 children lacking one or more antibody types after the customary 3-dose injection regimen resulted in all 12, who had possessed antibodies against one type of virus prior to the first injection of vaccine, becoming "triple positive," except for one child who lacked type 3 antibody. Of the remaining 27 children who had been "triple negative" prior to vaccination, 85, 100, and 56% possessed antibody types 1, 2, and 3, respectively, after the 4th dose.

The Epidemiology of Aseptic Meningitis and Related Nonspecific Disease in Connecticut, 1957: Virological and Clinical Studies. L. Dubin and D. M. Horstmann. Yale J. Biol. & Med. 30:429-441 (June) 1958 [New Haven, Conn.].

During the summer of 1957, virological and serologic investigations were carried out on specimens from 56 patients in Connecticut in whom nonparalytic poliomyelitis, aseptic meningitis, or nonspecific febrile illness had been diagnosed, and from 1 patient with paralytic poliomyelitis. It was possible to make a specific etiological diagnosis on 33 of the patients. The absence of poliomyelitis virus was striking. Only 2 isolations of the type 1 virus were made. This experience is in line with what occurred in the rest of the United States and is markedly different from the experience of the preceding years.

ECHO and Coxsackie viruses played a definite role as the etiological agents of aseptic meningitis and associated nonspecific febrile disease in various parts of Connecticut during the summer of 1957. In addition, agents not belonging to any of the known enterovirus types were also active in the same area at the same time and were associated with clinical syndromes similar to those produced by ECHO and Coxsackie viruses. ECHO virus type 9 was the most commonly isolated enterovirus, a finding which differs markedly from the Connecticut experience of the previous 2 years. An unusual clinical feature of the cases studied was the presence of a rubella-like rash, associated not only with ECHO 9 virus infection, but with Coxsackie A-9 and with unidentified agents as well. The rash was similar in character and distribution in the 3 etiological groups.

BOOK REVIEWS

Principles of Internal Medicine. Editors: T. R. Harrison and others. Third edition. Cloth. $18.50. Pp. 1782; 57, with 211 illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1958.

This book is becoming one of the standard textbooks in its field. The necessity for a third edition within eight years is evidence of its reception. As the book has proceeded through these editions, additional editors have been added to achieve uniformity of approach. For the new edition, the unconventional arrangement, as compared with other books in the field, has been retained but modified. New sections have been added by experts in their fields. The list of contributors is extensive and impressive. It encompasses most of the major medical schools in the United States and a few from abroad. The book begins with a short section on the approach to the patient by the physician. Part 2, "Cardinal Manifestations of Disease," takes up individual symptoms or signs from a broad medical point of view. The section on disorders of nervous function has been expanded and strengthened. Part 3 considers biological phenomena, such as inheritance, aging, neoplasia, and metabolic pathways, and the principals of electrophysiology. Part 4 systematically discusses metabolic and endocrine disorders, part 5, those due to physical and chemical agents, and part 6, those due to biological agents—the infectious diseases. Part 7 contains a short discussion of allergic diseases and drug reactions; Part 8 takes up the various organ systems. The last part is a general discussion of the care of the patient and covers principles of nutrition, sedation, and transfusion, as well as production of disorders by the physician.

Most of the sections are excellently written. The format, with narrow margins and two columns on a page, is pleasing to the eye and can be easily read. Scattered through the book are tables of particular tests comparing normal values with those found in specific diseases, as well as tables for comparison of effects of lesions. At the end in an appendix are tables of laboratory values of clinical importance. Six excellent color plates of patients and lesions are scattered through the book. A small number of clear illustrative diagrams is also included. The references at the end of each section are carefully selected, are few in number, and include articles through 1956. This book should serve well as a textbook for medical students and, for general practitioners and internists in practice, as a reference work.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Mirror to Physiology: A Self-Survey of Physiological Science. By R. W. Gerard, M.D., Ph.D., Sc.D., Professor of Neurophysiology in Psychiatry and Physiology, University of Michigan, Ann Arbor. Cloth. Pp. 372, with illustrations. American Physiological Society, 9650 Wisconsin Ave., Washington 14, D. C., 1958.

This book gives the results of a survey undertaken by the American Physiological Society in an effort to define physiology, to discover what kind of people are now classified as physiologists, and to consider how to interest an adequate proportion of the nation's manpower in cultivating this important field of science. In the foreword, W. O. Fenn expresses the belief that, if there is any serious deficiency in physiology at present, it is probably in the recruitment of personnel of high competence. Much space is devoted to the technical problems of the survey itself, and this should be instructive to other organizations planning similar ventures. Quantitative data were obtained as to the activities, employment, and income of physiologists, their occupational motivations, satisfaction, and mobility, and their research activities and programs. There are chapters on research facilities and support, publications and societies, professional training and recruitment, and public relations and education. A closing chapter interprets the results and makes recommendations. It is followed by an appendix and an index. This book represents an earnest and costly effort to define and count some extremely elusive entities. It is hard to say how successful this effort has been, but its importance is undeniable. This survey of one aspect of our scientific manpower problem deserves the attention of everyone who may be in a position to direct the engaging of personnel or the application of funds for teaching and research.

A Modern Practice of Obstetrics. By D. M. Stern, M.A., M.B., B.Ch., and C. W. F. Burnett, M.D., F.R.C.S., F.R.C.O.G. Second edition. Cloth. $9. Pp. 258, with 141 illustrations, line drawings by Susan M. Robinson. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; Baillère, Tindall & Cox, 7 & 8 Henrietta St., Covent Garden, London, W. C. 2, England, 1958.

This new edition of an English textbook of obstetrics was written for candidates for examination and practitioners of obstetrics. The authors indicate that, where there have been differences of opinion as to procedure, they have relied on their own

clinical experience. The result is a concise, practical book from which much theoretical and questionable material has been omitted. The subjects are logically presented in nine separate sections and an appendix in the following order: normal and abnormal pregnancy, normal and abnormal labor, the puerperium, operative obstetrics, the newborn baby, radiology, and maternal and fetal mortality. Informative and skillfully executed line drawings profusely illustrate all the subjects. The book includes a great deal of useful information concerning patients and benefits of state insurance and other matters of interest chiefly to the English practitioner. There are some differences in the accepted practices in Great Britain and those current in the United States, but fundamental principles are the same. Natural delivery is recommended in all cases unless operative procedures are indicated. Most obstetricians in the United States prefer to terminate labor by an episiotomy and outlet forceps after the head begins to bulge the perineum. An intelligent approach to abdominal delivery and the management of most complications is presented. The use of the external version to correct breech presentation in late pregnancy carried out with the patient under anesthesia, however, is questionable. The induction of labor in patients who are two weeks post-term and have babies of 6 lb. (2,721 kg.) or more in weight is not uncommon in Britain but is rarely practiced in the United States. It was a real surprise to read that paste can be introduced into the uterus as a method of therapeutic abortion. The format of the book, an appropriate quotation from Shakespeare which heads each chapter, an interesting cover, and legible printing add much to its appeal. It can be read with profit by American physicians as well as those in Great Britain.

Industrial Hygiene and Toxicology. Volume I: General Principles. Frank A. Patty, editor. [To be in 3 volumes.] Second edition. Cloth. $17.50. Pp. 830, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88/90 Chancery Lane, London, W. C. 2, England, 1958.

The revised edition of this treatise on industrial hygiene and toxicology has been expanded to three volumes. Volume 1 deals with general principles and contains chapters by the editor and 17 contributors. To keep abreast with the extension of industrial hygiene into new fields, chapters on human engineering and industrial safety, industrial sanitation, air pollution, industrial noise and the conservation of hearing, lighting for seeing, and heat control in the hot industries were added. Extensive revisions were made in the chapters on industrial hygiene records and reports, the pulmonary dust diseases, radiant energy, and ventilation. The remaining chapters required less extensive revision. This volume contains a wealth of useful and authoritative information in the various specialties. Many pertinent references are given to the original literature. The revised edition more than ever is an outstanding reference source and textbook for students and practitioners in the field of industrial hygiene and toxicology.

A Symposium on Non-Toxaemic Hypertension in Pregnancy. Edited by Norman F. Morris, M.D., M.B., B.S., Reader in Obstetrics and Gynaecology, University of London, London, and J. C. McClure Browne, B.Sc., M.B., B.S., Professor of Obstetrics and Gynaecology, University of London. Cloth. $8.50. Pp. 243, with 78 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W.1, England, 1958.

This symposium was held in London in July, 1957. The topics discussed included genetic studies of hypertension in pregnancy, the course of pregnancy complicated by essential hypertension, renal hypertension and pregnancy, pheochromocytoma, coarctation of the aorta and pregnancy, and the recognition and management of these conditions. The subject is presented as well as could be expected, considering the gross inadequacy of the existing scientific data. One is impressed by how far the obstetric field is behind in its understanding of hypertension. Still more discouraging is the fact that so little is being done to correct this inadequacy. A few of the more interesting points under discussion centered around the controversy as to whether a distinction can be made between a normal and hypertensive arterial pressure level. It is the old problem of trying to equate a disease with a single clinical sign. McMichael clearly disagrees with Pickering, who is a proponent of the statistical view. Duff concludes that the increased peripheral resistance in essential hypertension does not involve the upper extremities and does not depend on structural vascular narrowing or on overactivity of the sympathetic nerves, but these are rather large conclusions for the evidence submitted. The high incidence of gestoses in England is surprising. It is not made clear by Milne how mecamylamine differs completely from the quarternary ammonium blocking agents, although his vignette of the pharmacology of antihypertensive drugs is excellent. Theobald believes that weekly antenatal care is associated with a sharp fall in the incidence of eclampsia. It is hard to believe that the veratrum used in the good old days at Queen Charlotte's really did as much good as Mr. Bourne suggests. Any symposium on hypertension is the better for having Dr. Robert Platt in attendance. This one was no exception. Max Rosenheim, in his concluding remarks, hopes for another similar symposium. This would be worthwhile only if fresh data were forthcoming to arouse and sustain both interest and purpose.

QUESTIONS AND ANSWERS

PROGESTERONE FOR OVARIAN CYSTS

To the Editor:—*Please comment on the rationale of using oral progesterone therapy for small painful cysts of the ovaries. These cysts frequently occur, cause a lot of abdominal discomfort, and sometimes alter the menstrual cycle. Are there any references to this subject in the literature? Would treatment with cyclic estrogens help the condition? I am now giving progesterone orally during the last half of the menstrual cycle. Could such treatment have a salutary effect?*

Samuel S. Lambeth, M.D., Maryville, Tenn.

Answer.—The administration of progesterone produces a progestin effect on estrogen-primed endometrium and a suppressive effect on luteinizing hormone from the anterior pituitary. If the etiology of the small painful cysts of the ovary is endometriosis, the administration of progesterone should aggravate, rather than improve, the condition.

In most instances multiple small cysts of the ovaries represent a number of unruptured graafian follicles secondary to either an oophoritis which mechanically prevents ovulation or a functional disturbance of the pituitary-ovarian cortex axis. Clinically, this is most often manifested by altered menstrual cycles. Pituitary gonadotropin suppression by large doses of estrogen in regulated cycles sometimes produces symptomatic relief. Several aspects of the effects of endocrine therapy are discussed in the *American Journal of Obstetrics and Gynecology* (vol. 75, Jan., Feb., 1958).

CHEESE AND SERUM CHOLESTEROL LEVEL

To the Editor:—*Would the eating of 1.5 lb. of cheese a week—not cream cheese—tend to bring about an excess accumulation of cholesterol in a patient's system? What suggestions should be made to such a patient?*

M.D., North Carolina.

Answer.—There is no evidence to implicate the ingestion of 1.5 lb. of cheese a week with the development of an excess amount of cholesterol in the blood. There are so many variables concerned with the amount of cholesterol present in the body that one cannot blame any one dietary item. At the present time, there is no good evidence indicating that a high blood cholesterol level is a sign that one will have a heart attack. Apparently, there is a statistical relationship between high blood cholesterol levels and heart attacks, but, as yet, there has been shown no cause and effect relationship. The Food and Nutrition Board of the National Research Council has recently published a pamphlet in which this conclusion is made: "Evidence to support the concept that high levels of plasma cholesterol, per se, in man are atherogenic is far from conclusive. Circumstantial evidence, however, indicates that the kind, or amount, of dietary fat is in some way related to some stages of atherosclerosis in man. A reduction in intake of the more saturated fats in the diet may ultimately prove desirable for health but is not yet mandated by currently available evidence."

VENOUS SPIDERS

To the Editor:—*Please comment on the small, superficial, radiating types of varicosities so often seen on the anterior and posterior surfaces of the thighs of young women. This condition is encountered from time to time in individuals who are concerned only because of the cosmetic defect which it presents. Seemingly there is no relationship to the tendency towards varicosities in the lower extremities because it is so often seen in the absence of this finding in a great number of patients. Treatment by injection of sodium morrhuate with tiny (30-gauge) needles has been suggested. I have also tried electrolysis of some of these tiny vesicles, but the results have been equivocal, and the treatment is also painful. Should a young patient with such varicosities continue dancing and drill team activities?*

Harold L. Boyer, M.D., Las Vegas, Nev.

Answer.—Venous spiders appear on the thighs of women independently of varicose veins. Their mode of production is obscure, although a hormonal influence is suggested by their accelerated appearance or growth at puberty, during pregnancy, and after menopause. They frequently radiate from a small central pool. Venous spiders do not cause pain or swelling, they will not ulcerate, and they do seem to run in families. Occasionally, without any obvious injury, they rupture subcutaneously causing a small hematoma and much fear of blood clot.

There seems no reason to prohibit dancing or any athletic activity. Injection of the central pool with a few drops of mild sclerosing solution, with use of a magnifying glass, has been done. The spiders,

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

however, will appear somewhere else. Cautery is inadvisable and leaves a more unsightly scar than the original lesion. Parents, of course, are anxious to prevent any spread of such lesions. Nothing is known to this consultant which would effectively prevent new crops of spiders. Repeated pregnancies definitely aggravate them. Skin preparations may effectively cover them and relieve some of the anxiety relating to their cosmetic appearance.

PROPTOSIS

To the Editor:—*A 41-year-old woman stated that a fluorescent tube (20-watt) exploded in front of her right eye and that powder and glass entered this eye. Four days after the accident, both lids of the right eye were swollen; they remained so, and about two months after the accident bulging of the right eye began to develop. Examination revealed a proptosis of the right eye of about 5 mm., compared to the left. External examination showed bulging of the right eye; conjunctival hyperemia and chemosis of moderate degree; pupil equal, regular, and reactive to light and accommodation; and no limitation of ocular movements in all directions. Findings in fundoscopy were negative. Her vision is 20/20 in each eye. Results of x-ray of the orbits, including optic canals, were negative. Findings in all tests for thyroid function were also negative. The condition appeared clinically to be pseudogranuloma of the orbit. Please give information as to whether the chemical contents of the fluorescent bulb, as described below, can cause this type of condition: argon gas, very small amount under 3 mm. of pressure; liquid mercury, 50 mg.; fluorescent powder on wall, 5 Gm. of calcium halo phosphate (red), zinc silicate (green), and magnesium tungstate (blue) (although all lamps would contain all of these, the proportion would change depending on the color of the particular lamp); and emission coating at each end of filament, 12 mg. of calcium carbonate, barium carbonate, and strontium carbonate.*

M.D., New Jersey.

Answer.—The mention in the query of a "pseudogranuloma" at once suggests the action of beryllium. Not since 1949 has beryllium entered the standard brands of fluorescent tubes for illumination. There remains the unlikely prospect that an old tube might have been involved. The somewhat precise chemical analysis presumably would have detected beryllium if any had been present. Of the mentioned phosphors, none is known to be capable of inducing the significant findings indicated, notably the proptosis. Several are capable of inducing temporary acute irritation such as was observed. The action of tungsten on the human body, including that on the eye, has not been well explored. There remains the remote possibility that this one substance might be more active than is now established. In general, there is no known reason to attribute the proptosis to the action of the chemicals noted and under the circumstances set forth.

NYLON SENSITIVITY

To the Editor:—*A patient develops a contact dermatitis every time she wears nylon stockings or other pieces of clothing containing nylon. Is there any treatment other than elimination of nylon clothing? Can an antigen be made for injection? If so, where can it be obtained?*

Frank D. Levy, M.D., Philadelphia.

Answer.—There is no real effective prophylactic treatment for contact dermatitis due to wearing apparel such as nylon, apart from avoidance. Although commercial allergy laboratories prepare extracts of nylon for skin testing and presumably for treatment, desensitization with this material is questionable and has not met with great success. Before a recommendation is made that all types of nylon be discarded, however, a patch test should be performed in order to determine whether it is the nylon, the dye, or other chemicals used in the processing of the material which is responsible for the dermatitis. The technique of the patch test is described in textbooks on allergy and dermatology. Briefly, it consists of the application of a small piece of the suspected material on a convenient portion of the skin of the patient to be tested, covering with an occlusive dressing, and leaving the material in place for at least 48 hours. A positive skin test will be indicated by a dermatitis at the site of contact. Occasionally the reaction may be delayed. Therefore, it is wise to observe the site where the nylon was placed for several days after removal of the patch. Various colors and types of nylon material and nylon thread should be tested individually in order to determine which type, if any, can be used.

TREATMENT OF MUMPS IN ADULTS

To the Editor:—*Please outline therapy for mumps in a 30-year-old woman. Are antibiotics indicated and will they prevent encephalitis or pancreatitis?*

MD., Illinois.

Answer.—The treatment of a 30-year-old woman with mumps is symptomatic and supportive. Such general measures include rest and relief of pain with analgesics if necessary. Local application of heat or cold may help. There are no significant dietary measures. Headache and symptoms due to increased cerebrospinal fluid pressure occurring in encephalitis due to mumps may be relieved by reducing the pressure toward normal by lumbar drainage. Antibiotics are not indicated, nor will they prevent any of the complications of mumps, including

encephalitis and pancreatitis. Gamma globulin prepared from blood collected from patients in the convalescent stage of mumps has been shown to decrease the incidence of orchitis in adult males when given 24 hours or less after the onset of parotitis. Gamma globulin not specifically obtained from patients in convalescence from mumps did not have this effect. Definitive knowledge of the ability gamma globulin obtained from persons in convalescence from mumps to lower the incidence of involvement of the central nervous system or glands other than the parotid in females is not available. The value of steroid hormones for preventing or treating complications of mumps is not established.

PIGMENTATION OF THE GUMS

To the Editor:—*A 16-year-old boy has marked, dark pigmentation of the gums, such as is ordinarily seen in Addison's disease. However, there are no symptoms of this condition. His 17-ketosteroid level is within normal range, and a 24-hour excretion was doubled with the use of ACTH. There is no evidence of heavy metal poisoning. Laboratory studies, such as we are able to do, are within normal range. What other conditions should one consider with increased gum pigmentation in a boy of this age?*

Howard P. Holt, M.D., Yakima, Wash.

Answer.—Pigmentation of the attached gingival tissues, and at times the oral mucosa and lips, will develop in any dark-complexioned patient. This physiological pigmentation usually develops fully during the second decade. This pigmentation is the result of the deposition of increased amounts of melanin. Oral mucosal pigmentation may also be found in patients with intestinal polyposis. It may be present in the familial form of polyostotic fibrous dysplasia (Albright's disease). The administration of certain drugs, for example, quinacrine hydrochloride, may be associated with a yellowish pigmentation of the oral tissues. In the absence of any clinical or roentgenologic findings suggestive of intestinal polyposis or polyostotic fibrous dysplasia, it is most likely that the gingival pigmentation is physiological.

VITAMIN A INTOXICATION

To the Editor:—*Please give advice on what danger, if any, there is in the use of vitamin A. A recent article in an eye, ear, nose, and throat journal gave the impression that vitamin A intoxication could cause intracranial changes.*

M.D., Michigan.

Answer.—Apparently, the body can tolerate quantities of vitamin A 100 times greater than the daily physiological requirement, but there is a definite possibility of harm from the prolonged ingestion of vitamin A in excess of 50,000 I. U. daily. Chronic vitamin A intoxication occurs more frequently in children than in adults. Depending on the severity of the intoxication, the symptoms appearing in children older than 1 year include anorexia, loss of weight, extreme irritability, fretfulness and pruritus, seborrhea-like cutaneous eruptions, fissuring at the corners of the mouth, and cracking and bleeding of the lips. Later symptoms often include hepatomegaly, hydrocephaly, alopecia, painful swellings over the long bones with bone and joint pains and bone tenderness, hyperostosis, deep, hard, and tender swellings in the extremities, cortical thickening in tubular bones, and elevated serum vitamin A levels. Vitamin A intoxication in adults presents symptoms similar to those of hypervitaminosis A in children but usually milder. Structural bone changes are not likely to occur, and bone and joint pains are not so severe. Menstrual alterations, exophthalmos, and pigmentation of the skin are often found. Transitory hydrocephaly is a prominent finding when toxicity is acute.

NUMMULAR ECZEMA

To the Editor:—*A 19-month-old boy has suffered since the age of 8 months from a dermatosis classified as nummular eczema. The lesions are localized on both cheeks, shin, extensor surfaces of extremities, gluteal area, and abdomen. These well defined, reddish brown plaques tend to ooze and to form brownish scabs. There is a slight scaling, no itching, and some infiltration. Fungus studies have not been done. Various modes of treatment have been tried, including that with coal tar and other tar preparations, hydrocortisone cream and lotion, immune globulin, and antibiotics according to culture and sensitivity tests from the skin and from a concomitant chronic tonsillitis. The dermatosis is improved, with healing in the center of the plaques and less exudation; however, it is far from "cured." A few years ago a report appeared of treatment of nummular eczema with vitamin A given parenterally. Has this treatment proved successful? How is it done? Please give other suggestions as to the management of this case.*

M.D., Maryland.

Answer.—Nummular eczema is seen in children, but less often than in adults. In both, it is often resistant to treatment. Vitamin A therapy has been suggested by some, but its value in this condition seems limited. When vitamin A is used, parenteral therapy is usually not required. The danger of vitamin A intoxication should be remembered, especially in infants. In order to guard against this, there should be definite rest periods when vitamin A therapy is discontinued. From the morphologic description given, the diagnosis of infantile eczema should be considered.

BILIARY CIRRHOSIS AND COLITIS

To the Editor:—*A 28-year-old woman with massive ascites, abnormal liver function tests, and characteristic x-ray and proctoscopic findings of extensive ulcerative colitis involving all segments of the colon has been seen for the first time. There was 8,000 cc. of clear fluid removed from the abdomen for symptomatic relief. Have there been any recent experiences, in this uncommon situation, with respect to (1) efficacy of steroid therapy and (2) removal of the colon, presupposing that it is the site of the basic disorder and that the hepatic dysfunction is secondary?*

Robert C. Lawson, M.D., Oklahoma City.

Answer.—Biliary cirrhosis is not an uncommon late complication of long-standing ulcerative colitis. It would be of interest to know how long this patient has had the colitis, presupposing that the condition is of this type. In the absence of any evidence of malignant disease, however, this is the likely complication. Surgery at this stage is carried out with considerable risk, and it is not likely to revert the process in the liver. Steroid therapy has not proved to be of particular value in these cases.

CALCIUM AND ARTERIOSCLEROSIS

To the Editor:—*A patient with an ulcer says he has read that diets containing large amounts of milk predispose to arteriosclerosis. He blames this on the calcium content, not the fat content. Is there any substantiation to this?*

Robert M. Michels, M.D., Flushing, Mich.

Answer.—This consultant is unaware of any evidence implicating calcium in the development of arteriosclerosis. Some workers believe that an excessive consumption of animal fat, of which milk fat is one example, does have a causal relationship with atherosclerosis. However, this relationship has not yet been proved.

DIGITALIS AND NITROGLYCERIN IN MYOCARDIAL INFARCTION

To the Editor:—*Are digitalis and nitroglycerin indicated in treatment of acute myocardial infarction?*

Reynaldo E. Laureano, M.D., Baltimore.

Answer.—The use of nitroglycerin is not indicated in cases of known acute myocardial infarction. There is no reason to suppose that this drug will relieve the ischemia produced by an occluded vessel. In addition to this, nitroglycerin produces a fall in blood pressure which is not desirable in the shock state that may accompany myocardial infarction. Digitalis is not indicated for the treatment of acute myocardial infarction. If there is ventricular hyperirritability shown by frequent ectopic ventricular systoles, the use of digitalis is hazardous. However, if there is acute congestive heart failure associated with the infarction, digitalis should be used as in any case of congestive heart failure. Here digitalis is used in the treatment of the congestive failure, not in the treatment of the infarct. There is some evidence that digitalis may have an adverse effect on the coronary flow, but, in the presence of congestive failure, the hazard associated with the failure is greater than the hazard of a possible reduction in the coronary flow.

PRURITUS WITH CIRRHOSIS

To the Editor:—*A patient with hypertrophic (Hanot's) cirrhosis has a markedly elevated cholesterol level of 2,000 mg.%, an elevated bilirubin level of 10 mg.%, and a main complaint of severe pruritus. She has not responded to the usual therapeutic procedures and medication. Please advise treatment for both the primary disease and the pruritus.*

Roy T. Pearson, M.D., Spokane, Wash.

Answer.—There is no specific treatment for hypertrophic cirrhosis. It is desirable to maintain adequate nutrition, and it is important to provide extra amounts of the fat soluble vitamins, since these are poorly absorbed in this condition. Medical treatment of the pruritus is usually rather ineffective. Animal charcoal given orally three or four times a day is sometimes effective. Dihydroergotamine, given by injection, is sometimes helpful, but it is important not to use it too frequently because of possible toxic effects. Prolonged T-tube drainage of the common duct is sometimes necessary and usually relieves the itching.

BREAST FEEDING AND DEODORANTS

To the Editor:—*A mother who is breast feeding her infant has had great variations in milk supply. She believes that her use of a deodorant and antiperspirant has caused marked reduction in the available milk. Abstinence from the antiperspirant has apparently allowed an adequate flow of milk within 36 hours. Is there any available data on this subject?*

Mack J. Mosely Jr., M.D., Galveston, Texas.

Answer.—The quantity of breast milk that becomes available during the period of lactation is dependent, in the main, upon (1) the inherent ability of the lactating glands to secrete and (2) the ability of the infant (or pump) to completely empty each breast at least three times within 24 hours. It seems quite conceivable that during the application of deodorants and antiperspirants in the axillas, sufficient material reaches the breasts and nipples to provoke a distaste so that the infant does not empty the breasts, which then quite promptly secrete less. It seems very doubtful that the external and superficial application of such material exerts a direct antigalactagogue action.

FORMALDEHYDE HAZARD

To the Editor:—*In the Questions and Answers section of* The Journal *for Aug. 23, 1958, page 2157, a physician inquired about formaldehyde hazard resulting from the manufacturing of the new resinate wash-and-wear garments. I would add to the reply of the consultant that there has been considerable difficulty with irritation, presumably from the formaldehyde vapor, in retail establishments selling these garments. Such difficulty usually occurs only during warm weather, and as soon as cooler temperatures prevail there is no longer any difficulty. The problem that has shown up has been one primarily of irritation of the skin and nasal mucosa. Such a situation has recently been reported from the Baltimore Health Department. There is apparently some dispute about the exact reason for the plant closing in Phoenix, Ariz., to which the inquiring physician referred. There is perhaps some question as to whether the illness actually resulted from employees handling urea-formaldehyde resins.*

Mitchell R. Zavon, M.D.
University of Cincinnati College of Medicine
Cincinnati 19.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*As earlier noted, when polymerization of urea-formaldehyde resin is complete no untoward effects are expectable. In the application of this resin together with the catalyst to textile material, complete polymerization is not always achieved. In some situations this occurrence may be accidental; in others it may be deliberate. In the formulation of this resin some excess of formaldehyde may be provided. One stated reason is that this excess masks the ammonia odor of urea or, to the same end, paralyzes the odor receptors within the nasal mucous membrane. The chemical form of the formaldehyde may be uncertain, but through absorption or adsorption of this gas or a compound thereof it is retained in or on the fibers. This may be influenced by the quantity of the catalyst applied. The group of workers most likely to be affected are garment workers from fabric earlier treated. Some difficulty may continue to the wholesale and retail trade. In department stores the elevated temperature of summer does not per se increase the exposure. Indirectly the situation derives from elevated temperature, in that department stores provide air conditioning with complete recirculation of air. This recirculation tends to build up the formaldehyde level. The commonest manifestation is eye inflammation from direct irritation. More serious situations, such as dermatitis or asthma, may be attributed to allergic response to formaldehyde sensitization.*

MAGNESIUM SULFATE DRESSINGS

To the Editor:—*In the Questions and Answers section of* The Journal, *May 3, 1958, page 145, there was a question concerning the use of magnesium sulfate dressings. The answer given concerned a discussion of osmosis—the action of hypertonic salt solutions in causing fluid to flow from areas of lesser to greater osmotic tension. This is all well and good; however, the most important aspect of osmosis, that is, the semipermiable membrane, was not mentioned. If it was meant to be implied that the unbroken epithelium acts as a semipermiable membrane, then this is a new concept to me. As an ophthalmologist I make frequent use of hot soaks to the eyelids; however, I have always felt that the heat with its vasodilating properties was the only beneficial aspect of this type of therapy.*

Capt. T. J. Tredici, Scott Air Force Base, Ill.

The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*The fact that heat causes superficial vasodilatation in no way proves augmentation of blood flow in the underlying inflamed area. Recent studies (Lewis,* J. Physiol. **140:285, 1958**) *correlate the reversal of inflammation with the formation, within the inflamed area, of pharmacodynamically active polypeptides with vasodilating and permeability altering properties. The peri-inflammatory fibrinous membrane is highly effective in preventing the entry of blood, antibodies, prescribed antibiotics, etc., (Dubos, Biochemical Determinants of Microbial Diseases, Cambridge, Mass., Harvard University Press, 1954) into the target zone. Even if heat did get by the fibrin barrier, how could it eliminate such mechanical barriers to small vessel blood flow as interstitial edema and the vascular and lymph compressive effects of dense inflammatory exudation?*

The key factor in reversing inflammation, in the opinion of this consultant, is a change in the permeability or, more properly, the impermeability of acutely injured tissue. This constitutes the basic rationale for the anti-inflammatory effects of systemically administered proteolytic enzymes (Innerfield, Ann. New York Acad. Sc. **68:167, 1957**) *and, indeed, the application of soaks or wet dressings.*

Continuous wet applications have a macerative effect on the skin, thereby injuring and altering the permeability of the interepithelial cement matrices. Actual penetration and seepage of applied fluid to the inflamed zone is the basic aim of soaks. When successful, increased permeability of the inflammatory membrane occurs and drainage ensues. The justification for making the solution hot would be the factor of increasing blood flow after modification of tissue impermeability had been achieved.